STERILISATION BY STEAM UNDER INCREASED PRESSURE

A REPORT TO THE MEDICAL RESEARCH COUNCIL BY THE WORKING PARTY ON PRESSURE-STEAM STERILISERS *

DURING the past few years a number of incidents and reports published in the medical and lay press have suggested that pressure-steam sterilising procedures followed in hospitals have not been achieving a satisfactory standard of efficiency, and that there is a need both to define the performance required of such sterilisers and to consider how it can be attained (Thiel, Burton, and McClemont 1952, Bowie 1955, Howie and Timbury 1956, Howie 1956, Scott 1957, Nuffield Provincial Hospital Trust 1958). In May, 1957, the Medical Research Council set up a working party to examine this question, and this report presents their findings and recommendations.

The report is based on a number of extensive and detailed investigations into existing arrangements for the sterilisation of surgical equipment in hospital wards, surgical units, sterile-supply departments, laboratories, and pharmacies. These have shown that the situation in this country is as unsatisfactory and unsafe as that in United States hospitals, as described by Walter (1948). While it has revealed a number of technical causes contributing to the inefficiency of sterilising processes, it has also shown that the underlying factor responsible for the situation as a whole is a widespread lack of understanding throughout the Health Service of the exact conditions required for efficient sterilisation and for the safety of those who operate sterilisers. It is to this aspect of the situation as much as to any other that the Working Party wish to draw attention.

PRINCIPLES OF STERILISATION BY STEAM UNDER INCREASED PRESSURE

The need for sterilisation by steam under increased pressure arises from the fact that the spores of many common and dangerous bacteria are strongly resistant to dry heat. The most effective way of killing the spores is by means of steam at high temperature and high humidity which will condense into their substance and moisten them thoroughly.

To bring about this effect all parts of the load to be sterilised must be free of air, so that it may be permeated by the steam; and the steam must be not only hot—at 120° or 130°C—but nearly saturated; that is, it must be at a pressure so high that in spite of its high temperature it is close to the point of condensing to liquid water. Steam in this condition is termed " just dry ". Departures from this condition, to be discussed later, result in inefficient sterilising operations.

In medical work steam sterilisers are mainly used for:

(*a*) Surgical dressings and other packaged goods.
(*b*) Unwrapped instruments and bowls.
(*c*) Surgical rubber gloves.
(*d*) Bottled fluids.

For the preparation of sterile water and saline some hospitals use a tank type of steriliser; this is discussed below.

The necessary conditions for steam sterilisation are most difficult to meet in the sterilisation of dressings, since it is not easy to remove air from the pores of close-packed fibrous material. Most of this section is therefore concerned with the problem of sterilising textiles, with particular reference to dressings.

Removal of Air

The removal of air is the first essential in the sterilisation of textiles. There are two methods in general use, the " high-vacuum " method and the " downward-displacement " (or gravity-displacement) method, and two corresponding types of steriliser.

THE HIGH-VACUUM METHOD

From a high-vacuum steriliser air is removed by a powerful pump which reduces the absolute pressure of air in the chamber to a value of a few millimetres of mercury column before steam is admitted. This is often described as drawing an almost perfect vacuum, and it means removing more than 98% of the air initially present.[1]

It must be emphasised that this is the only method of sterilisation that can overcome the effects of bad packing or overloading of the steriliser (Bowie 1958a, Knox and Penikett 1958).

Degree of Vacuum

Cotton or any other hydrophilic material left in a constant atmosphere will take up or lose water until equilibrium is reached—i.e., until the vapour pressure of water over the material equals the actual partial pressure of water in the air. If the material is then placed in a steriliser chamber and the pressure is reduced there will be little loss of water until the point is reached where the absolute pressure in the chamber equals the equilibrium vapour pressure over the material. At this point the water will " boil " out, sweeping the residual air ahead of it. This absolute pressure constitutes a vacuum sufficient to start the process of sterilisation. Evidently pressures need to be lower for cold dry conditions than when they are hot and moist.

The pressure of water vapour in equilibrium at 15°C with cotton containing 4% by weight of water (and substantially lower humidity is unlikely to prevail in normal conditions in this country) is about 5 mm. Hg (communication from British Cotton Industries' Research Association [Shirley Institute]). In theory a pump capable of drawing a vacuum of this high order is necessary. In practice preliminary vacua of a slightly lower order may be acceptable. Knox and Penikett (1958) for example, reported satisfactory results only when their vacuum reached a level of 20 mm. Hg absolute pressure, and some manufacturers and users are content with an " almost

1. In this country the degree of vacuum is commonly expressed in inches of mercury column. We have retained this usage in parts of our text where those most interested would be more familiar with this form. In other parts of our text, where high-vacuum apparatus is described, measurements are given in terms of absolute pressure in mm. of mercury. For convenience the following table gives approximate equivalents of these two usages in terms of each other.

VACUUM CONVERSION TABLE

Degree of vacuum	Absolute pressure	
(in. Hg)	(in. Hg)	(mm. Hg)
29·5	0·5	12·5
28·0	2·0	50·0
25·0	5·0	125·0
20·0	10·0	250·0
15·0	15·0	380·0

* The members of the working party are: Prof. J. W. HOWIE, M.D. (chairman); Dr. V. D. ALLISON; Dr. J. H. BOWIE; Dr. E. M. DARMADY; Prof. R. KNOX, M.D.; Dr. E. J. K. PENIKETT (until November, 1958); Dr. J. A. V. SHONE; Mr. G. SYKES, M.SC.; Mr. C. D. WEIR, PH.D. (until May, 1958); Prof. C. A. WELLS, F.R.C.S.; Mr. G. A. P. WYLLIE, PH.D.; and Dr. J. C. KELSEY (secretary. Address: Department of Bacteriology, Guy's Hospital Medical School, London, S.E.1.).

perfect vacuum ", which is in practice a vacuum of the order of 50 mm. Hg absolute pressure (Bowie 1958a and b). More experimental evidence is clearly required.

It appears that the efficiency of this process of air removal increases with the proportion of the chamber volume occupied by the material, since the more material there is, the more water vapour is available to remove less air.

Effect of Oxygen Removal

Since oxidation kills spores it might be assumed that sterilising efficiency is reduced by the complete removal of air. The available evidence (Savage 1944) suggests that the effect of removing air is equivalent to a drop in temperature of less than 1°C.

DOWNWARD-DISPLACEMENT METHOD

In a downward-displacement steriliser the air is removed from the load by gravity—i.e., it is allowed to trickle out under its own weight (Bowie 1955, Perkins 1956). More precisely, the difference in density between cool air and hot steam, of the order of 1 mg. per c.cm., gradually forces the air downwards out of the load.

It must be emphasised that this method will render contaminated material sterile *only* if the steriliser is skilfully operated, carefully packed, and not overloaded.

Use of Vacuum

Many existing downward-displacement sterilisers are fitted with steam ejectors capable of withdrawing 30-50% of the air from the chamber. This so-called vacuum is sometimes drawn two or more times, steam being admitted between each vacuum, before sterilisation is actually begun.

Clearly, if air and steam mix well before the vacuum is again drawn, the air content will drop progressively, in fact by geometrical progression. This condition can usually be met in sterilising gloves, bowls, instruments, and bottled fluids, so that the practice is worthwhile in that application. On the other hand, in the pores of a textile material air and steam mix very slowly, so that successive low-order vacua (15 in. Hg or less) merely produce a " breathing " motion of the same air inside the material. Thus in the sterilisation of dressings one or more pre-vacua of this low order are not worth drawing; indeed it is wasteful of costly steam and less efficient than good downward-displacement. Furthermore no time is saved, and since it is not possible to predict the rate of air removal from the material in the steriliser the temperature in the chamber drain cannot be taken as a reliable indication of the temperature inside the load. Between high-order vacua (greater than $29^1/_2$ in. Hg) of whose value there is no doubt, and these low-order vacua (15 in. Hg or less) which we consider ineffective, the possible applications and usefulness of intermediate-order vacua await definition.

Packing of Material and Penetration by Steam

The pressure difference pushing the residual air out after steam has been admitted is comparable in degree with, though working in the opposite direction to, the draught developed in a short chimney over a feebly burning open fire. Therefore, to appreciate the rate of air removal from, say, a packed drum, it might be compared with the rate at which the gases from such a fire would pass through such a drum if it were jammed upside down in the chimney. Clearly, then, in downward-displacement sterilisers the load must be loosely packed, and arranged so that no pockets of cool air can form within it. Even so it will generally be necessary to allow a penetration time of fifteen minutes or more while the steam is flowing into the chamber and air is escaping from the load in large amounts; so that it is essential to make provision for the continued automatic removal of air and condensate from the chamber, and to ensure that it works; when the penetration time has been completed the sterilising period can be said to begin.

A skilled operator can sterilise perfectly reliably with such apparatus, but the conditions for success must be strictly observed, and the task should never be entrusted to untrained staff.

Quality of Steam

The quality of steam is known to vary with the degree of saturation, the amount of water-fog carried in it, and the amount of air it contains. As has already been mentioned, it is an essential requirement for steam sterilisation that the steam should be " dry ". In practice this is achieved by means of a steam separator in the supply pipe just in front of the entrance to the reducing valve, and is entirely an engineering matter.

The available evidence suggests that steam of a dryness fraction above 90%—i.e., having less than 10% of its weight made up of liquid water—is acceptable for sterilisation. Steam that is wetter than this is likely to result in inefficient sterilisation (see below).

Trouble may also arise through superheating, a condition in which the steam is hotter than saturated steam at the same pressure, as discussed by Walter (1948).

For the purposes of sterilisation the maximum acceptable upward deviation for steam in contact with spores is a temperature of 5°C.[2] Cotton materials that are not sensibly damp at the outset have the characteristic of adsorbing water so strongly that even if the steam entering the steriliser is saturated there will be a superheat of 3°C or more in the interstices of a cotton load. No additional superheat must therefore be allowed, and accordingly the common practice of running the jacket at a temperature up to 10°C hotter than the chamber is strongly deprecated.

The superheat just described exists in pure steam: in a superficially different sense superheat may exist in air-steam mixtures.

Thus a mixture containing 10% by volume of air, at 121°C and 15 lb. per sq. in., contains steam at 121°C and a partial pressure of $13^1/_2$ lb. per sq. in. This pressure in pure dry saturated steam corresponds to a temperature of only 118°C. On cooling at constant pressure this mixture will shed no water and so will yield no latent heat of condensation until it has cooled by the necessary 3°C. Therefore in a steriliser containing such a mixture it is not possible to ensure that the temperature in any part of the load is within 3°C of the external temperature. A temperature drop of 3°C in (now saturated) steam corresponds nearly to a doubling of the sterilising time, which is outside the margin of safety.

The situation described here is not just a theoretical one but it is one which can exist in a steriliser when the removal of air is incomplete and the pressure is maintained by the incoming steam. The air-steam mixture will meet cool parts of the load but will not begin to transfer heat to them until it has lost 3°C. It is therefore wise to ensure that the air content of the steam in any part of the load should not exceed 5% by volume during the sterilising period.

It must be emphasised that this *does not* mean that only 95% of the air need be removed from the steriliser at the outset, for the steam entering a mass of cotton will push the air ahead of it to form a central " bubble " of nearly pure air, which is very slow to diffuse out. Such a bubble will prevent sterilisation of the dressings in contact with it. In practice under correct conditions of packing and loading it will be displaced slowly by gravity.

Timing

When the steam has reached the correct temperature, sufficient time must be allowed for the physical changes that kill the bacteria and their spores to take place through-

2. A wider deviation may be tolerable at the highest temperature (134°C), but experimental evidence on this is still decidedly inadequate.

out the load; it is these changes that constitute the sterilising process.

Times corresponding to different temperatures have been given by Perkins (1956) as follows:

2 min. at 132°C	18 min. at 118°C
8 „ „ 125°C	30 „ „ 116°C
12 „ „ 121°C	

To allow for deviations in steam quality a further (safety) period is added. Adapting Perkins' figures (above) to the pressures most commonly employed, we recommend the following times and temperatures as a minimum:

3 min. at 134°C (30 lb. per sq. in.)
10 „ „ 126°C (20 „ „ „)
15 „ „ 121°C (15 „ „ „)

Damage to Spores and to Materials

The deterioration of cotton and rubber and the inactivation of bacterial protoplasm are not wholly dissimilar processes, and efficient sterilisation depends largely on achieving the latter while keeping the former to a minimum.

As the steam temperature rises, the time required for killing resistant spores falls faster than does the time required for doing a given amount of damage to cotton. Consequently, were the sterilising period the only consideration, sterilisation would be best effected at the highest temperature available. As regards pressure, however, the size and cost of autoclaves make it undesirable to operate at above two atmospheres gauge pressure for general-purpose sterilisers.

It is probably uneconomic to reduce the sterilising period much below the time required for steam to penetrate the load, so there is little point in running a downward-displacement steriliser above 126°C; at the same time there will be little point in spending money on doubling the pump speed of a high-vacuum steriliser in order to improve upon a pumping-down time of about four minutes, when the holding time is itself about four minutes for a sterilising temperature above 130°C.

Because it requires a longer period for steam penetration, retains more oxygen, and has a lower working temperature, a downward-displacement steriliser gives rise to more damage to goods per sterilising cycle than a high-vacuum steriliser, even when it is operated with equal care.

The question of damage is not of great importance if materials are to be used only once and then discarded; and there is much to be said for placing responsibility for the sterilising of such goods on the manufacturer, if subsequent contamination can be avoided.

Drying

At the end of a sterilising run it is necessary to dry the load without recontaminating it.

The state of dryness of the load will be fixed by the equilibrium established between the vapour pressure over the load and the pressure in the chamber—the lower the chamber pressure the more rapid will be the " boiling off " of the water. At this stage practically no air should be present in the chamber, and, since only steam with very little permanent gas needs to be removed, a water jet pump is specially suited to do this effectively and rapidly. Such a pump need be of quite simple design, for small sterilisers at least, and a vacuum of 28 in. Hg can readily be attained. In practice, the vacuum of 20 in. Hg obtainable by an efficient steam ejector will usually give satisfactorily dried dressings from a modern downward displacement steriliser, but only if a dry steam supply can be guaranteed. The usefulness of a water jet pump on such sterilisers seems not to be sufficiently widely known.

If the dressings have not been made grossly wet by inadequately dried steam, the mere attaining of the vacuum should be sufficient to achieve drying without a need to maintain it. Henry (communication from the Shirley Institute), and Penikett, Robson, and Rowe (1958) found that with a high-vacuum steriliser operated with dry steam, the load was back at its starting condition, as regards temperature and humidity, at the end of the sterilising cycle.

Air must be admitted to break the vacuum before the steriliser is opened. This air must be drawn from a clean source through a bacteriological filter (see below).

THE COMMONEST FAULTS AND THEIR TREATMENT

Seven main faults affect the efficiency of sterilisers used for surgical dressings and rubber gloves; these will be discussed in turn. It is emphasised that these faults apply only to the operation of the downward-displacement type of equipment commonly in use, and not to the modern high-vacuum steriliser. Indeed, the installation of a high-vacuum steriliser would provide a satisfactory remedy for most of the defects discussed.

Use of Wet Steam

Wet steam is a frequent cause of incomplete sterilisation. It causes the dressings in the steriliser to become soaked with moisture, usually early on in the sterilising process, so that they become less amenable to steam sterilisation by downward-displacement. Moreover, the subsequent drying of the wet dressings is a lengthy process which is damaging to rubber gloves and some other materials, and when it is accomplished by prolonged airing it carries a serious risk of recontamination by airborne organisms.

Wet steam is usually caused by inadequate lagging, inadequate condensate trapping, and inadequate separation in the steam supply pipe. In some sterilisers this defect may be overcome by the installation of a steam separator in the supply pipe just in front of the entrance to the reducing valve.

Incomplete Penetration of the Load

There are three main causes of inadequate penetration of the load by steam:

Retention of Air and Condensate

In many sterilisers there are no arrangements, or no reliable arrangements, for the automatic removal of air and condensate from the goods during sterilisation. Unless air and condensate are removed, the sterilising process cannot be fully effective in any steriliser, and will be particularly ineffective in all sterilisers which rely upon downward-displacement of air with or without the partial vacua attainable with steam ejector mechanisms—that is to say, in almost all the sterilisers in use in surgical units in Britain today.

The fitting of an efficient automatically operated near-to-steam trap (Northcroft 1956) is not a difficult procedure in sterilisers which have a discharge channel. Sterilisers which have no such channel—and even today these are not rare—cannot safely, and in reasonable time, sterilise packaged goods intended for surgical operations. It is sometimes possible to fit discharge channels to such sterilisers; but, since most of them have other serious faults of design, it is usually advisable to replace them.

Every chamber discharge channel should be of adequate diameter and fitted with a non-return valve and a readily visible sight-glass showing the flow of condensate. A continuous flow of condensate indicates to the operator that the discharge channel is open. The channel should drain into a tun-dish (which should be removed far enough from the steriliser to prevent free steam from being a nuisance); the

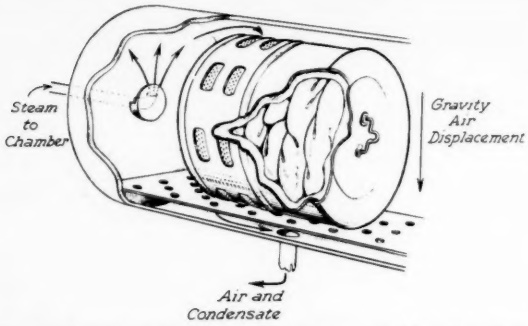


Fig. 1—Correctly packed drum with open ports positioned to allow gravity air displacement. (See section on the Use of Packs instead of Drums.)

air-break provided by the tun-dish will ensure that there will be no reflux contamination from drains—a remarkable but not unknown phenomenon (Bowie 1955).

Overloading of Drums and Caskets

Steam cannot penetrate thoroughly into the contents of drums and caskets that are tightly packed. It is apparently not generally understood that a drum which can only be closed with difficulty is grossly overpacked. The articles in a drum must fit loosely together and be laid flat. To avoid the formation of air pockets, sheets of mackintosh or jaconet should be interleaved and rolled with some permeable fabric, so that no two surfaces of the non-permeable material are in contact. Even with this precaution, mackintoshes may fail to be sterilised.

Incorrect Positioning of Containers in the Sterilising Chamber

Sterilisers are often incorrectly loaded, as many containers as possible being crammed into the chamber irrespective of the position of the ports. In downward-displacement sterilisers this practice renders the sterilising process completely unreliable. The ports or vents of the container must always be fully open during sterilisation, and the container itself should be so positioned in the steriliser that steam can flow through it by way of the open ports from top to bottom without impediment (fig. 1). In addition, the dressings or other material in the container must be so packed that when the container is correctly positioned in the steriliser the folds in the fabric run vertically; there will then be no obstruction to the natural downward displacement of air by steam.

If the steam pathway is correctly directed, the drums loosely packed and correctly positioned, the discharge channels adequate, properly trapped, and fitted with a thermometer, then, and only then, can a simple downward-displacement steriliser be efficiently run.

Incorrect Timing of Sterilising Runs

A common fault is that sterilisers are run for periods of from two to five hours. These long cycles destroy gloves and other heat-sensitive materials and add nothing to the efficiency of the sterilising operation. Furthermore they reduce the sterilising capacity of the unit, which, in turn, leads to over-packing, and sometimes to postponement of sterilising operations until the night staff come on duty. Thus it may happen that junior and inexperienced members of staff may be left in charge of a process which they do not understand.

A correctly timed sterilising run is one that will ensure that all parts of the load are held at a sufficient temperature for a time adequate to kill bacteria and their spores. The exposure time consists of the sum of (1) the penetration time, during which steam permeates the load and raises all parts of it to the required temperature; (2) the holding time, which is the minimum time known to kill spores at this temperature; and (3) the safety period, which in the downward-displacement steriliser is usually about half the holding time. The following recommended minima for combined holding time and safety period have already been mentioned:

3 min. at 134°C
10 „ „ 126°C
15 „ „ 121°C

For operations in which packing and loading are satisfactorily accomplished and a fully efficient steriliser is correctly operated, the following table indicates the exposure times required at 121°C and 126°C using downward displacement for the removal of air:

	121°C (15 lb. per sq. in.)	126°C (20 lb. per sq. in.)
Instruments and utensils ..	15 min.	10 min.
Fabric packs	30 „	20 „
Dressing drums	45 „	30 „

The run should be timed from the moment when a thermometer correctly placed in the discharge line reaches a temperature within 2–3°C of that corresponding to the chamber pressure. A thermometer placed in the centre of a dummy load of standard composition and suitably positioned would probably provide an even truer reading of the temperature in the chamber.

At the end of the timed exposure period, if the steam and dressings were dry at the outset, and the load was correctly packed and positioned, all that is required to dry the dressings is to draw a vacuum of about 20 in. Hg. There is no need to hold this vacuum for five to ten minutes, as is sometimes advised. Should it be found necessary to do so, wet steam or an incorrectly packed load should be suspected. Thus the whole operation will require a total duration of around sixty minutes at the longest, in marked contrast to the overlong runs of two to five hours mentioned above.

With high-vacuum equipment the total sterilisation time can be greatly reduced, a complete cycle taking as little as twenty minutes (Bowie 1958a). The penetration time is greatly reduced, because after an almost perfect vacuum has been drawn, steam permeates the load almost instantaneously. Also, with a minimal penetration time a high sterilisation temperature may usefully be employed, with a consequent reduction in the holding time and safety period. Thus, at 134°C, under ideal conditions, an accurately timed exposure period of three minutes is adequate. These higher temperatures cannot usefully be employed with downward-displacement equipment, since the long penetration time would mean that the outside of the load would be damaged before steam had reached the inside.

Incorrect Treatment of Gloves

The instructions given to staff often stipulate that surgical rubber gloves should be exposed at some 10 or even 5 lb. per sq. in. for periods of fifteen minutes or less. Such exposures cannot guarantee sterility, and their widespread use should cease. In at least one outbreak of postoperative tetanus the gloves were "sterilised" differently from the rest of the packaged goods and were the only articles, among many known to be contaminated with tetanus spores, which were not cleared of these organisms by the procedures intended to produce sterility.

From experiments specially conducted for this investigation we are satisfied that if gloves are properly packed

—that is, on their sides, with slips of gauze inside the wrists to facilitate steam penetration, and in correctly loaded containers (fig. 2)—they may be treated at a pressure of 20 lb. per sq. in. (126°C, 259°F) for an exposure period of fifteen minutes. With an initial period of five minutes for the chamber-drain temperature to reach its required value, and with a drying period also of five minutes, the gloves are safely sterilised during a run of twenty-five minutes.

Under these conditions solution-dipped surgical gloves are still usable after 6 runs, although they are by then showing signs of oxidation. Survival for 6 such sterilisations represents the life specified for such gloves. The hardier latex-dipped gloves show virtually no signs of deterioration after 6 such exposures, but some surgeons dislike latex-dipped gloves because they lack elasticity, do not give so sure a grip, and take up water; if this type of glove could be made acceptable to surgeons, the problem of glove sterilisation would be considerably reduced. Solution-dipped gloves are obviously more delicate, but even they will have an acceptable period of usefulness if properly sterilised.

Our evidence suggests that high-vacuum, high-pressure sterilisers permitting very brief exposures of gloves at 130°C or over probably combine safety with the minimum deterioration (Bowie 1958a and b, Schmidt and Moller 1954).

Recontamination of Sterilised Loads

Recontamination can undo the work of a sterilising operation before or after the load is removed from the steriliser. Before removal, and during the drawing of the drying vacuum, a faulty non-return valve in the chamber drain can lead to the aspiration of dirty air where a tundish airbreak is provided, or of dirty water where it is not.

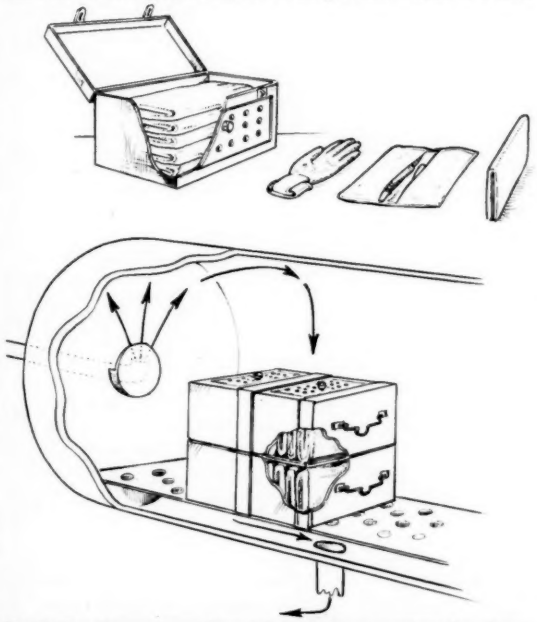


Fig. 2—Top figure shows, from left to right, a container for gloves properly packed ready for insertion into a steriliser; a glove folded and lined with gauze; a pair of gloves packed in fabric envelope; and a fabric envelope on edge to show its correct position during the sterilisation.

Lower figure shows a container as actually loaded in the steriliser. Note that the envelopes are set on edge by turning the container so that the steam passes directly from above downwards through the holes. The air and condensate are discharged below through the vent.

A more common cause of recontamination is an inadequate air filter.

Recontamination During Drying

In many hospitals it is the practice to dry dressings by drawing warm filtered air through them for periods which appear to range from eighteen minutes to several hours. The longer periods are sometimes due to forgetfulness on the part of the operator, but they are sometimes adopted because the dressings have been allowed to become soaked during sterilisation, so that prolonged drying is required to render them acceptable to the surgeon. For this purpose drying periods of one to three hours are common. (We have heard of one hospital where drying was being completed by leaving the drums with their ports open on top of a hot water radiator.)

The outstanding drawback to this practice is that with the filtration methods currently employed it is technically extremely difficult to ensure the sterility of the air drawn into the steriliser. In the first place its temperature is often in the region of 56°C, and since dry air at this temperature has little if any bactericidal power the sterility of the air depends on the efficiency of its filtration. In the second place many sterilisers have no provision for filtration of air: others provide filters which do not merit the name.

In many sterilisers the filters are maintained by the occasional insertion of pieces of cotton wool or other fabrics. Sometimes these are well chosen, adequate in size, and carefully sterilised. Much more often the filter cup contains an ill-fitting plug of dirty cotton wool—or nothing. In such circumstances dressings have been found to be contaminated with a great variety of bacteria, including most often saprophytic staphylococci and diphtheroids, but also, and not infrequently, *Staphylococcus aureus* and *Clostridium welchii* (Howie and Timbury 1956).

At present the best known way of avoiding recontamination during drying is to ensure that the dressings are dry at the outset, to use dry steam, and to draw a vacuum of 20 in. Hg after sterilisation. The vacuum need not be held even for five minutes (see sections, above, on Drying and on Incorrect Timing of Sterilising Runs) as is commonly advised, and should be broken by admitting air from a clean source through an air filter. The filter may be a metal cup which should be filled with a dry sterile plug of slag wool or non-absorbent cotton wool; this should be replaced daily and never allowed to become wet. Specially designed filters with or without a cotton wool plug may prove more satisfactory (Rice 1958).

In addition to the main air inlet many sterilisers have one or more petcocks connecting the chamber with the exterior; obviously these must also be provided with efficient air filters.

Recontamination during Removal, Transport, and Storage

A load may become contaminated during its removal from the steriliser, in transport, and during subsequent storage in wards or theatres. In some wards 23% of the dressings have been found to be contaminated (Darmady et al. 1959).

After sterilisation a typical sequence of events is as follows:

As the drums cool, air from the surroundings is drawn through the ports and through the space between the lid and rim. After a variable interval the vent over the ports is closed. The drums are hot, and a rough pair of gloves or a heavy duster or piece of sacking is commonly used to handle them; the attendant is not dressed in sterile clothing, nor does he wear a cap or mask. Frequently the drums are old and dented, so that the ports can be closed only with difficulty if at all, and the gaps between the ill-fitting lids and the rims afford a permanent

means of entry for the dust of the sterilising room—which is often sited near a source of gross dirt. For these various reasons it is essential that there should be protective material covering the ports inside the drums.

When the drum is opened, in theatre or ward, the protective material is either discarded or folded back. In either case there is a grave risk of further contamination, either immediately or on subsequent reopening. This may take place simply through contact with the surrounding air, by means of the forceps used for the removal of individual articles from the drums, or through the nurse who removes or uses the articles.

The Operation of Sterilisers by Uninstructed Staff

It will have been seen that steam sterilisation is a complicated technical procedure requiring not only that the apparatus should be in good working condition and not of obsolete design, but also that the operator should have a thorough understanding both of the underlying principles and of the practical procedures involved. There is a clear need for these important matters to be made the responsibility of a single member of the medical staff.

In practice, however, most surgeons assume the sterility of all goods treated in pressure-steam sterilisers. In effect they almost always delegate responsibility for the working of the steriliser to the theatre superintendent, and through her to nursing staff or attendants. It is a fault of present-day arrangements that the specialised knowledge of the engineer and of the bacteriologist is not regularly used to support that of the nursing staff in the supervision of sterilising procedures.

More often than not the engineer is only called in when things are visibly wrong, and his main concern is often simply to ensure that the apparatus fulfils safety requirements. Similarly, bacteriologists may not be called in until treated dressings are found to be contaminated. Even then they may mistakenly base their advice on their experience with laboratory or pharmacy autoclaves, which are simple to operate, and so overlook the much greater problems involved in sterilising dressings.

Laboratory autoclaves are mostly used for sterilising media, fluids, and unwrapped instruments and bowls, and they do this with a gratifying efficiency which, moreover, is automatically checked, at least for bacteriological media. A flask of fluid or agar medium in a laboratory autoclave producing steam under pressure of 15–20 lb. per sq. in. will be sterilised in fifteen minutes or less, even if there is no gravity discharge mechanism to get rid of the air. Such a procedure is not comparable with the complex operation involved in effecting the penetration by steam of a load of dry surgical dressings so that all air is displaced and steam of sterilising quality reaches every fibre of every article of the load.

Nursing staff tend to apply in all circumstances the sterilising methods they were taught when first instructed in the use of surgical sterilisers. We know of many instances where potentially efficient sterilisers were being wrongly operated according to a card of instructions clearly modified to fit the ideas of someone who had not realised that sterilisers are not all alike. Reports have also been received of junior nurses suffering or narrowly escaping serious accidents through opening or trying to open the doors of sterilisers containing steam still under pressure. Evidently, then, the tuition of staff needs greater emphasis as regards both the general principles of sterilisation and the detailed operation of different types of sterilisers.

Concerning the latter, an immediate improvement could be effected by the relabelling of all valve-control handles on existing sterilisers with their names (e.g., " steam to chamber "; " air filter "; " vacuum ", and so forth), instead of with letters or numbers. It would then be possible to issue unequivocal and standard instructions at least on the general principles of operating a steriliser of any reasonable pattern with some degree of certainty that the instructions would not be reduced to confusion by the different functions of control handles labelled A, B, C, or 1, 2, 3, on different sterilisers. Indeed, where complicated and dangerous pieces of apparatus are likely to be operated by persons who are not familiar with the procedures involved, a sound precaution is to make their operation as fully automatic as possible, and it is recommended that this should be applied to sterilisers.

Defects of Installation and Maintenance

It is of great importance that sterilisers should be correctly installed and that there should be adequate arrangements for their maintenance. At the present time the development of defects is usually unforeseen and breakdowns are therefore not prevented. This situation would be improved by the provision of more trained maintenance staff.

DEFECTS IN INSTALLATION

Defects observed include:

1. *Incorrect Siting*

Sterilisers should be installed only in places that are clean and free from obvious sources of infection. Theatre suites are not the places for sterilising dressings because these may be contaminated initially with spores and other micro-organisms.

2. *Steam Supply of Poor Quality*

The pressure head of steam is often too low or inconstant, heat insulation may be absent or insufficient, and condensate trapping or separation inadequate. The supply pressure at the site of installation, whether the steam is generated in a boiler-house at some distance from the steriliser or in a high-pressure boiler adjacent to it, should be constant and at least 20 lb. per sq. in. above the pressure used in the steriliser.

3. *Incorrect and Insanitary Connections with Service Pipes*

Air breaks should be provided at the steriliser, so that there is no direct connection between the steam jacket or chamber discharge channels and condensate returns, water mains, and common drain pipes.

4. *Inefficient Steam Venting or Condensing*

In many sterilisation rooms, waste steam from sterilisers, instrument boilers, and similar apparatus is discharged directly into the room. This not only causes much damage to walls and ceilings, but, what is more important, it permits breaks in aseptic technique; with pressure-steam sterilisers the discharge is often noisy and disturbs the surgeon.

5. *Unhygienic Mounting*

Sterilisers should preferably be built into a cabinet or panel, and not mounted in the open as is commonly the case; they should, however, be easily accessible to inspection. When sterilisers are " built in ", the ventilation shafts of the recess or cabinet should be conducted to atmosphere outside that of the theatre suite, and not directed backwards into the sterilisation room.

6. *Insufficient Sterilisation Space*

This is very evident, particularly with regard to packaged equipment such as casketed or wrapped dressings for use in busy surgical units. Since most existing dressing sterilisers are cylindrical and deep, usable space is still further reduced and loading and unloading is awkward.

DEFECTS IN MAINTENANCE

Defects in maintenance include:

1. *Lack of Cleanliness*

Arrangements seldom exist for the regular cleaning of either boilers or sterilisers for instruments and bowls. Steriliser

chambers, discharge channels, chamber walls and fittings, and headring drains all require regular attention; many air-filter cups are never opened.

2. *Instruments Out of Order*

Pressure gauges may not function properly, either because the hollow "Bourdon" tube is punctured, or, more often, because the gearing has been out of adjustment for a long time, so that the indicating pointer never reaches gauge zero and the pressures indicated are always several pounds per square inch too high. Similarly recording thermometers and pressure gauges may often remain out of adjustment for long periods. Records of pressure are sometimes misleadingly translated into temperature by the incorrect use of temperature charts with pressure-sensitive recording apparatus. It appears that indicating thermometers and temperature recorders are seldom checked at regular intervals with a standard thermometer or with the pressure gauges of the steriliser.

3. *Leakages in Gaskets, Stop Valves, and Safety Valves*

Such leakages are often allowed to persist for very long periods before adjustment, repair, or replacement by the engineer.

4. *Blocked Discharge Channels*

These blockages are often due to the accumulation of foreign matter. Sleeves and steam strainers are generally dismantled only after the channel has become choked—in spite of the fact that they are specially designed for easy maintenance. Steam traps are seldom checked for correct functioning, and really efficient "near-to-steam" traps are mistakenly replaced by traps designed for heating apparatus other than autoclaves. At least one outbreak of postoperative tetanus has been proved to be due to a blocked discharge channel (J. W. Howie, personal communication).

5. *Damaged Door Fittings*

Hinges, gears, and other door fittings, including safety mechanisms, are seldom tested for efficiency or maintained in proper functioning order, but are repaired only when they become unworkable. Lack of maintenance work on doors not infrequently leads to such dangerous practices as the use of a lever to secure or open a steriliser. It should perhaps be emphasised that inspectors employed by insurance companies dealing with sterilisers are concerned with the safety of the steriliser—not with the safety of the operator or with steriliser design in relation to sterilising efficiency.

SOME MISCELLANEOUS QUESTIONS

The Sterilisation of Instruments

Small pressure sterilisers that are efficiently designed and operated are wholly preferable to boilers for the sterilisation of clean instruments. For one thing they eliminate all temptation to dip an instrument in water presumed to be boiling and hurry it to a waiting surgeon. The dangers implicit in such a practice are not fully realised. If traditional instructions to boil for twenty minutes were to be faithfully observed, the advantages of sterilising instruments for a few minutes in small pressure-sterilisers would soon be fully recognised.

On grounds of function and economy, pressure-sterilisers to be used only for the sterilisation of unwrapped instruments and bowls need not be of rectangular form. For routine use with a loading carriage inside the chamber a convenient size is approximately 24 inches in diameter and 40 inches in length. If the apparatus is to be used only for the emergency sterilisation of a dropped or forgotten instrument, the size may be limited to approximately 8 inches in diameter and 22 inches in length. A steam jacket is not essential, but its use enables the operator to complete the process of sterilisation more rapidly. Since air in the chamber and between individual articles of the load is easily and rapidly flushed from the chamber by way of a suitable vent and bleeder valve [3] on the discharge channel, and since the load may be flash-dried after sterilisation, a preliminary vacuum for the extraction of air or a vacuum for drying the load after sterilisation is unnecessary, and, in fact, prolongs the process time. In general-purpose, high pre-vacuum pressure sterilisers, however, there is no other objection to the use of these vacua; the use of a 28 in. Hg vacuum for drying results in rapid cooling of the load.

The most suitable design for instrument and utensil pressure-sterilisers is more simple than that of any other form of steam steriliser—other than the cheapest domestic pressure cooker—and many sterilisers in existing theatres may be converted with ease to this specialised use (Bowie 1958 b). Provided instruments and bowls are clean, the appropriate process of sterilisation merely involves the transfer of heat and humidity to the freely exposed solid surface of the load. There is no need to allow time for steam penetration and "heating up"; so the chamber pressure gauge and the discharge-channel thermometer are safe guides to the conditions of exchange at the load surfaces. From the time the chamber thermometer indicates the temperature selected for sterilisation, the total requisite holding period for sterilisation and for a suitable safety margin is confidently recommended as fifteen minutes at 121–123°C or as three minutes at 132–134°C. These are the sterilising temperatures most commonly used; but it must be understood that they represent the two extremes of an acceptable range, limited on the one hand by excessive time and on the other by excessive cost. Within this range any convenient temperature may be used, provided that it is held for an appropriate time.

The process of sterilising unwrapped instruments and bowls is so simple and so rapid (less than five minutes at 132–134°C) that operation by means of manually operated stop valves is justified, although semi-automatic control (camshaft or multiport valve) is safer, and fully automatic control is safer still.

A typical operation of such a steriliser is as follows:

With jacket pressure gauge indicating 32 lb. per sq. in. (or 17 lb.), chamber loaded, door secured, and chamber vent open, steam is admitted to the chamber; air is extruded by way of the vent and the chamber is filled with steam more rapidly than could be effected by means of a preliminary vacuum. When the pointer of the thermometer has passed 100°C the vent is closed. The chamber pressure gauge indicates the rapidly rising pressure, closely followed by the thermometer. Residual air is evacuated through the discharge-channel bleeder. When the thermometer indicates 132°C (or 121°C), timing of the three-minute (or fifteen-minute) period of sterilisation is begun. When this is over the steam-to-chamber valve is closed and the chamber abruptly vented through a wide-bore discharge-channel or vent. When the chamber pressure reaches gauge zero the door may be opened; the unwrapped instruments and bowls dry instantaneously.

The Sterilisation of Bottled Fluids

The process of sterilising hydrated fluids is relatively simple, because any contaminating bacteria will already be moist and their destruction merely necessitates heating the fluid in each container to the appropriate temperature and holding it there for the appropriate time, e.g., 121°C for twelve minutes (Perkins 1956) or 115°C for thirty minutes (*British Pharmacopœia*). The usual procedure is:

1. To admit steam slowly through an inlet near the top of the chamber until the air in the chamber is displaced through the discharge channels in the bottom of the chamber and the temperature of the contents is raised to the required point.
2. To hold the temperature at this point.
3. To exhaust the steam to atmospheric pressure over a period of not less than ten minutes.

For convenience the steriliser should preferably be

3. On this type of steriliser an automatic steam trap, although effective, would be less rapid.

rectangular in shape and fitted with trays or a carriage on which the bottles may be placed. To avoid corrosion due to the spilling of liquids during sterilisation the chamber should be lined with nickel; alternatively it may be washed out thoroughly after each run or sprayed with a corrosion-resistant layer. No vacuum-producing apparatus is necessary, since downward displacement is quite satisfactory for removing the air, and drying is not required. It is not essential for the sterilisers to be jacketed provided they are efficiently lagged, and in this country many of our largest jacketed pressure steam vessels—often at present functioning inadequately as dressing sterilisers, particularly in central sterilisation rooms—could easily be converted for use as sterilisers for bottled aqueous solutions.

Where possible, sterilisers for bottled fluids should have multiple discharge channels, particularly if the chamber is large. These discharge channels may be fitted either with one or more near-to-steam balanced pressure traps (Northcroft 1956) or with a manually operated stop valve with or without a " bleeder " or by-pass. The heating-up time within the containers depends, of course, upon their wall thickness and volume. G. Sykes (personal communication) gives the following times as those required to heat containers of various sizes in flowing steam:

	Room temperature to 100°C	100°C to 115°C
100 ml. bottle	7 min.	3 min.
1 pint bottle	22 „	10 „
5 litre flask	40 „	15 „

In large containers heat " layering " may be present. Sykes found that in an 8-litre flask there was a twenty-five minute difference between the rates of heating in the top and bottom layers of the liquid. For this reason it is an advantage to have a thermometer actually in the fluid to be sterilised (Bowie 1958b); but, if such containers are being used repeatedly for bottled fluids, once an adequate cycle has been determined experimentally it can be controlled subsequently by the thermometer in the chamber drain.

Since bottled fluids may be required for intravenous injection it is essential that they should be pyrogen-free, and it is worth remembering that no amount of sterilisation will remove pyrogens from solutions already contaminated. Adequate steps should therefore be taken in the preparation of such fluids to ensure that they are not contaminated. This will also enable the minimum exposure period to be used; this is an important factor because a sterilisation cycle for bottled fluids takes considerably longer than one for instruments or fabrics. Unduly prolonged exposure periods should be avoided since deterioration of the properties of the solutions may result (Thiel et al. 1952).

In order to avoid excessive breakage due to heating or cooling the bottles too quickly, dialled flow-regulators may with advantage be fitted to the chamber steam inlet and to one of the discharge channels; thus the time taken to raise and lower chamber pressure before and after sterilisation may be controlled automatically (Bowie 1957). The appropriate intervals can again be determined by experiment with standard loads so that the regulators will not need further adjustment. It is, of course, possible, though probably less satisfactory, to control the sterilisation cycle by means of the more ordinary pattern of stop valve. In this case it is highly desirable that the position of the various valves (all of which should be clearly labelled with the function peroformed) should be standardised in relation to each other, and to the gauges and steriliser container.

The Tank Form of Steriliser

This type of steriliser was developed at a time when surgical teams were almost entirely self-supporting as far as the preparation of surgical equipment was concerned. Even the best designs are necessarily most complicated, and theatre staffs find their operation both lengthy and confusing. In any case, the continued sterility of the contents cannot be assured, since stop valves and delivery faucets cannot in practice be made bacteria-proof. In America they have long since been regarded as bacteriologically unsafe, and there they have now become obsolete owing to the supply of sterile fluids in bottles, including wash-basin fluids for the surgical team at the operating table. The bottles are stored within surgical suites in warming cupboards at temperatures suitable for immediate use; each bottle has a special pouring lip the sterility of which is preserved by a hermetically sealed cap (Perkins 1956) suitable for repeated use. On the Continent of Europe there has been a similar development, and we recommend the practice in this country.

The Use of Packs Instead of Drums

Wrapped packages of surgical dressings and other goods for use in the theatre and wards possess many advantages:

1. Two wrappings are used, the outer being handled by the " dirty " nurse, the inner being taken and handled only by the " clean " nurse.
2. There is no risk of aspiration of dust and air on cooling, since there is no rigid container.
3. Dressings or other materials sufficient for only one procedure are put in each pack, so the question of reopening does not arise.

The disadvantages of packs are:

1. More detailed packing is called for.
2. A relatively large number and variety of packs needs to be prepared and kept in hand.
3. Provision must be made for suitable cupboard space for their storage. These storage cupboards should have perforated shelves, close-fitting doors, and dust-proof vents, and they should be slightly warmed to ensure that they are thoroughly dry.
4. Care must be taken to exclude insects and to prevent contamination of the packs by wetting. This risk can be minimised by the use of such plastic wrappings as allow the passage of steam but not of water or bacteria.

It will be seen that the advantages of packs far outweigh the disadvantages, especially where the only dressing sterilisers available are of the downward-displacement type.

THE TESTING OF STERILISERS

From what has been said earlier it will be realised that the chamber-drain temperature record (or the temperature inside a standard dummy load) is the main indicator of whether a steriliser is working correctly and whether the load is receiving an adequate heat treatment. Even with a perfectly designed and completely automatic steriliser, and with correctly packed and positioned loads, there will always be occasions when a test of the overall efficiency of the sterilising process is desirable. There are two methods of testing: one uses bacteriological preparations, and the other uses chemical indicators.

Although in theory spore preparations provide the most realistic test, in practice the results may be dangerously misleading unless such preparations are carefully prepared and tested for heat resistance. The commonly used mesophilic organisms are unlikely to provide an adequate safety margin, and thermophils may be too heat-resistant and lead to needless rejection of a sterilising procedure. Soil samples are very variable and often too resistant. Satisfactory spore-papers can be made from *Bacillus stearothermophilus*, a non-pathogenic thermophilic organism; for spore-papers the minimum heat resistance should be five minutes at 121°C or one minute at 130°C. However, even with a satisfactory spore preparation there must be a delay of several days before the results of the test are known.

Chemical indicators have the advantage of being standard in performance and readable immediately the test is done. While the ideal chemical indicator has yet to be devised, the Browne's tube (type I—dressings) has been found by a number of authors to be satisfactory in the ordinary downward-displacement steriliser (Howie and Timbury 1956, Scott 1957, Alder and Gillespie 1957, Nuffield Provincial Hospitals Trust 1958). If used intelligently and stored correctly it probably provides the best routine test now available for this type of steriliser. There can be no justification for using a less exacting test for gloves (cf. section on Incorrect Treatment of Gloves), and in this respect the type-II Browne's tube is not recommended.

High-vacuum sterilisers are fully instrumented and automatically controlled, and once a sterilisation procedure has been laid down and checked with suitable spore preparations the temperature record should provide an adequate assurance of sterility. An additional safeguard is probably desirable; although at the high temperatures used, Browne's tube type I has too great a safety margin, and even the type II tube may be too insensitive, but it may be taken that if the latter turns green during a high-vacuum sterilising cycle a satisfactory heat treatment has been given.

In general, we suggest that spore preparations should be used only for assessing new techniques or equipment, for research purposes, and for occasions when a rigorous "full-dress" inspection is needed for administrative or forensic reasons. Such preparations must be of known resistance to heat. For routine tests with downward-displacement sterilisers chemical indicators should be used (Kelsey 1958).

In addition to tests for adequate sterilisation, tests for subsequent recontamination should be carried out from time to time (Howie and Timbury 1956), cf. section on Recontamination of Sterilised Loads; such tests can be done by culturing clean swabs placed in the outermost layer of the contents of packs or drums. If satisfactory air filters are provided this need not be a routine test.

It must be emphasised that a daily inspection of the temperature record by a responsible person is of more importance than the most elaborate laboratory tests carried out at long intervals.

REPLACEMENT POLICY

In deciding a policy for the replacement of inadequate equipment it is of course necessary to take account of any existing equipment and the uses to which it may still be put, as well as considering what new equipment is essential. In this section, therefore, the capabilities of the various kinds of sterilisers are summarised and examples are given of the ways in which the old equipment may best be used in conjunction with new.

Existing Equipment

Sterilising equipment currently in use in hospitals may be classified according to functional design:

1. *Boilers* of various kinds, operating at atmospheric pressure and used for instruments and utensils, and for water and saline.

2. *Tank forms of autoclaves* for water and saline.

3. "*Dressing sterilisers*".—In practice the instruments so designated include sterilisers of all shapes, sizes, age, and design. They are of great importance because they are used for the final preparation of all categories of medical and surgical equipment suitable for sterilisation by steam under pressure. It is a serious matter, therefore, that such sterilisers are often improperly designed, installed, operated, or maintained, and cannot therefore be relied on for the sterilisation of packaged loads.

4. *Modern steam sterilisers.*—These include:

(*a*) *Downward-displacement sterilisers* of specialised design used for:

(i) unwrapped instruments and utensils. These sterilisers are of horizontal cylindrical shape. Some are controlled by hand-operated stop valves, some by a single hand-operated wheel, and a few by automatic devices. Small sizes are suitable for the rapid processing of a single dropped or forgotten instrument, larger ones for routine use;

(ii) bottled fluids. These sterilisers are rectangular and their chamber capacity is generally greater than 25 c. ft.;

(*b*) *High pre-vacuum sterilisers* with automatic control, used according to size, as follows:

(i) small sizes for unwrapped instruments and utensils;

(ii) large sizes for packaged equipment (casketed or wrapped);

(iii) sizes of capacity up to 9 c. ft. are supplied as general-purpose sterilisers for all categories of equipment suitable for sterilisation by steam under pressure.

Procedure Recommended

It is considered advisable that all hospital boilers operating at atmospheric pressure and used for sterilising instruments and utensils should be replaced by pressure-steam sterilisers of type 4 (a) (i) or 4 (b) above; also that boilers and tank forms of autoclaves for water or saline should be replaced by type 4 (a) (ii), and conveniently located to serve the whole hospital. For the storage of sterile water and saline an adequate supply of bottles with special caps that preserve the sterility of the contents and of the pouring lip might be said to be a necessity.

Depending upon their design, size, and shape, existing and serviceable downward-displacement "dressing sterilisers" will be best employed in such places as ward preparation rooms, hospital laboratories, and pharmacies; in minor theatres that are used only once or twice a week; and for the disinfection of mattresses. Alternatively they might be converted, as appropriate, to fill one of the roles outlined in 4 (a) above. In this way, all serviceable sterilisers, many of them at present functioning inadequately as "dressing sterilisers", could be used to advantage for purposes within their operational capacity.

It is recommended that when new sterilisers are purchased those to be used for the treatment of packaged equipment should always be of the high pre-vacuum type, automatically controlled, and preferably rectangular in shape for more efficient packing. The proposed location will determine the size to be chosen, which, for efficiency, should not exceed approximately 26 c. ft. and probably not exceeding 9 c. ft. where the steriliser will be used for general purposes.

In output of sterile packaged equipment per hour, a well-designed, high pre-vacuum general purpose steriliser of 9 c. ft. (with essential automatic control) is equivalent to the most efficient downward-displacement steriliser of 40-50 c. ft., with or without automatic control; also, in high-vacuum apparatus, unnecessary damage to heat-sensitive materials is avoided.

Essential Features of the Modern Automatically Controlled High-vacuum Steriliser

General

Since the Working Party are of the opinion that the high-vacuum steriliser should replace many other types, the main requirements for its operation are outlined. It is essential that means should be provided for drawing a high-vacuum before admission of steam, and for maintaining at the same time a steam pressure of up to 34 lb. per sq. in. in the jacket, if one is present, and a vacuum

within a few mm. Hg of absolute pressure in the chamber. But this does not necessarily mean that the operating steam pressure need always be as high as 34 lb. per sq. in. For many purposes a pressure of 15–20 lb. held for slightly longer periods may be equally satisfactory.

The Chamber

There are obvious advantages in having machines of standard size, or of two or three standard sizes at most—the largest being about 25 c. ft. A rectangular chamber is the most convenient, and its dimensions should of course be such that containers of the most common sizes will fit it economically. The doors of the chamber (there may be one only or one at each end) should carry safety devices which make it impossible to open them when the chamber is under pressure, and they should also be insulated in such a way that the heat loss from the closed chamber is approximately the same in all directions. The chamber may be either steam jacketed or insulated.

The Steam

It would greatly facilitate the operation of sterilisers if manufacturers would undertake to state the range of variations in quality of steam within which each machine will operate efficiently. All machines should be fitted with devices to ensure that the steam entering the chamber is not superheated nor has a dryness fraction of less than 0·95, and that the steam entering the chamber is as free of air as possible. It is in any case essential that such devices should be attached permanently to the steriliser, so that its steam connections may be made to mains steam, a boiler, or its own generator. The jacket and the chamber must be supplied through the same reducing valve, or valves, set within the range 35–10 lb. per sq. in. The adjustment of these valves should not be possible by the operator. The condensate discharge pipe should be fitted with satisfactory means for air removal and for preventing reflux aspiration.

Air Removal

A pump should be provided which will reduce the absolute pressure in the chamber before the admission of steam to a very low figure. The figure suggested is 15 mm. Hg or below when the chamber is fully loaded with cotton fabrics containing 4% by dry weight of water, and having a temperature not exceeding 15° C. The pump should preferably be capable of reducing the pressure to this figure within five minutes. Such a pump will not remove all the air; but in practice, on the basis of temperatures actually recorded (Knox and Penikett 1958, J. H. Bowie, personal communication), it is acceptable. The steriliser is designed to ensure the removal of residual air continuously from the moment that steam is admitted to the chamber. In view of the difficulties discussed in the section on Removal of Air it is clear that more experimental evidence is required before standards of performance are rigidly defined.

Steam Removal

At the end of the sterilising operation the pump must be able to reduce the abolute pressure to 50 mm. Hg or less within five minutes. The same standard of performance should be possible after a number of successive runs.

Air Entry

A filter should be provided whereby sterile air can be admitted to the chamber after the removal of the steam. Apart from opening the door there should be no means of letting air into the chamber except through a device which ensures sterility.

Instruments

For the chamber, a large pressure and vacuum gauge and a large dial temperature gauge should be provided in positions convenient for easy reading. If two doors are provided two chamber-pressure gauges are required to prevent attempts from being made to open the door while the pressure within the chamber is still raised. An instrument for accurately reading absolute pressure in mm. Hg is required. The temperature gauge should have its sensitive element so placed that it records the lowest temperature in the chamber or load during sterilisation. A combined temperature, pressure, and vacuum pen-recorder operating from sensitive elements in similar positions to those operating the non-recording instruments should be provided. For the jacket, a pressure gauge is likewise required. Temperature and pressure gauges on the steam supply would be useful additions.

Controls

A simple control such as a wheel is the most suitable, and should be provided for automatic as well as for hand-controlled machines. In automatic machines, which are activated by sensitive elements which measure physical conditions within the chamber, the sterilising period must be controlled by the temperature of the coolest point in the load, and the exposure time must be in accordance with the accepted period for that temperature. Should there be a failure to achieve sterilising conditions, an alarm should sound and the chamber be vented to atmosphere. The pre-set controls should not be accessible to the operator.

Maintenance and Testing

It would be an advantage if manufacturers would provide with their machines a maintenance schedule and instructions for testing steam quality, gauges and the sensitive elements of instruments, and that where necessary—e.g., for testing steam quality—the necessary test valves were fitted to the machine.

Manufacturers might be encouraged to provide a monthly maintenance service, and to issue certificates of operational efficiency.

For a detailed discussion of the modern high vacuum steriliser, see Bowie (1958a).

Modification of Existing Sterilisers

Pending the replacement of downward-displacement sterilisers used for dressings by high-vacuum equipment, it is advised that every effort be made to upgrade them. By undertaking relatively simple modifications some can be made safe and effective. This may be done by carrying out ordinary engineering repairs, by fitting near-to-steam traps,[4] discharge-line thermometers, and air filters (Scott 1957), by running jacket and chamber at the same temperature, by providing a regular supply of dry steam, and by providing for a terminal vacuum adequate to remove steam from the chamber, thus ensuring simpler, quicker, and more thorough drying (Knox and Penikett 1958, Penikett, Robson, and Rowe 1958). Some sterilisers may be raised to high-vacuum status by the fitting of special pumps and automatic controls.

Some of the problems involved are helpfully indicated by Magee and Oakes (1958). These workers fitted a pump to a 120 c. ft. disinfector, with whose previous performance as a steriliser they were dissatisfied. The fitting of the pump produced considerable improvement although, as would be expected with so large a chamber, the results fell short of those

4. Such traps are now made by a number of manufacturers, who will advise on the choice of trap for any particular application. For recent studies on this subject, see Barson et al. 1958.

specified in this report as being attainable in chambers of 25 c. ft. or less.

CONCLUSION

It has been the aim of this inquiry to re-examine the requirements for efficient sterilisation by steam under pressure, and to discover how and why the conditions in many hospitals today apparently fail to meet them. An account is given of the principles and technical procedures of sterilisation by this method, and the more common defects leading to inefficient processing are described. Some immediately applicable remedies are described, and longer-term matters of policy are discussed.

It is the conclusion of the Working Party that while there are a number of causes contributing to inefficient sterilisation the underlying factor responsible for the situation as a whole is a widespread lack of understanding of the technical requirements involved. This in its turn is because no one member of the medical staff is given the final responsibility of ensuring the provision of suitable equipment and its proper use and control by specially trained operators. Until this is done, and until routine supervision of the sterilising apparatus by a member of the engineering staff is insisted upon, patients in many hospitals will continue to be exposed to the unnecessary hazard of infection caused by the use of imperfectly sterilised articles.

REFERENCES

Alder, V. G., Gillespie, W. A. (1957) *J. clin. Path.* **10,** 299.
Barson, T. E., Peacock, F., Robins, E. L., Wilkinson, G. R. (1958) *J. Pharm. Pharmacol.* **10,** 47T, 56T.
Bowie, J. H. (1955) *Pharm. J.* **174,** 473.
— (1957) *Hosp. Engr,* **11,** 246.
— (1958a) *Hlth Bull., Edinb.* **16,** 36.
— (1958b) *Hosp. Engr,* **12,** 158, 182.
Darmady, E. M., Hughes, K. E. A., Jones, J. D., Verdon, P. E. (1959) *Lancet* (in the press).
Howie, J. W. (1956) *ibid.* ii, 951.
— Timbury, M. C. (1956) *ibid.* p. 669.
Kelsey, J. C. (1958) *ibid.* i, 306.
Knox, R., Penikett, E. J. K. (1958) *Brit. med. J.* i, 680.
Magee, K. C., Oakes, H. E. (1958) *Hosp. Engr,* **12,** 278.
Northcroft, L. G. (1956) *Lancet,* ii, 790.
Nuffield Provincial Hospital Trust (1958).
Penikett, E. J. K., Robson, E., Rowe, T. W. G. (1958) *J. appl. Bact.* **21.**
Perkins, J. J. (1956) Principles and Methods of Sterilisation. Springfield, Ill.
Rice, H. M. (1958) *Lancet,* ii, 1275.
Savage, R. N. (1944) *Quart. J. of Pharm.* **17,** 165.
Schmidt, B., Moller, E. (1954) *Z. Hyg. InfektKr.* **140,** 144.
Scott, A. C. (1957) *Lancet,* ii, 633.
Thiel, C. C., Burton, H., McClemont, J. (1952) *Proc. Soc. appl. Bact.* **15, 53.**
Walter, C. W. (1948) The Aseptic Treatment of Wounds. New York.

ASPECTS OF PREVENTIVE CARDIOLOGY *

A. R. SOUTHWOOD

C.M.G., E.D., M.D., M.S. Adelaide, M.R.C.P., F.R.A.C.P.

CONSULTING PHYSICIAN TO THE ROYAL ADELAIDE HOSPITAL; LECTURER IN PUBLIC HEALTH AND PREVENTIVE MEDICINE IN THE UNIVERSITY OF ADELAIDE

(*Concluded from p.* 382)

II—THE RISE OF BIOCHEMISTRY

AN outstanding feature of 20th-century medicine is the advance of biochemistry. In that field are proceeding most of the present-day laboratory researches into atherosclerosis, and much may be expected from that biochemical approach.

Statistics on Atherosclerosis

In postmortem examinations of people over 50 years of age some intimal changes are to be seen in the arterial walls, although—even in the very old—the lesions may be slight in extent and degree, interfering little with the blood-flow. In life the condition may be practically symptom-free, recognisable only when obstructive complications come. We know atherosclerosis by its works, disturbing and often disastrous. Mortality figures give some indication, for nearly all cardiovascular-renal (C.V.R.) deaths in people over 50 are certified to be so caused. The fact that it is cessation of the heart-beat that constitutes the principal criterion of death doubtless accounts for some exaggeration of the number allocated to that category; cases of sudden death, for instance, are especially likely nowadays to be attributed to coronary thrombosis.

The need for caution when comparing figures from different countries has already been stressed. The range of crude death-rates (all causes) is from 767·7 (Netherlands) to 1206·0 (Belgium); rates for senility (B45) vary from 6·2 (New Zealand) to 225·9 (France)—for vascular lesions (B22) from 59·6 (Belgium) to 186·6 (Scotland). There are great differences, even in similar and often adjacent countries; but some of these are less significant than at first appears. They often reflect differences in the concept, reporting, and classification of causes of death (Lew 1957). The studies by Yerushalmy and Hilleboe are notable (1957).

The incidence of C.V.R. deaths in Australia for various age-groups is shown in fig. 9; the percentage change in several recent census years, using the year 1911 as the standard, indicates a continuing fall for all ages under 50, but increases for ages above that and for all ages combined. When, as shown in fig. 10, the figures for the senility and ill-defined categories (both small) are added to C.V.R. deaths, a decline in the rates is shown for every ten-year age-group, although the all-ages rate has increased—a curious possibility well known to statisticians.* Fig. 11 shows the rapid increase in Australia in the death-rate from coronary heart-disease since 1930. Fig. 12 shows the steady ratio of 2/1 in male/female death-rates from that cause for each year from 1940 to 1955.

Some investigators claim that the increase recorded in deaths from coronary heart-disease is largely an artefact. Lew (1957), for instance—reviewing a series of death certificates sent to the Metropolitan Life Insurance Company (New York)—finds that about 30% of the increase from 1940 to 1955 in the crude death-rate from coronary disease is accounted for by the greater proportion of old people, another 40% can be ascribed to statistical practices and classification, and most of the remaining 30% represents merely " the acceptance of a broader concept of coronary disease, better diagnoses, and increasing usage of the term coronary artery disease in certifying causes of death ". That is an extreme view. Most physicians think that deaths from coronary heart-disease, especially in middle-aged men, are commoner than they used to be.

* Being an amateur in statistics, I did not readily see how it could be possible for an increase in the death-rate for all ages to be compatible with a decrease in *all* of a series of subgroups. Playing with hypothetical sets of figures cleared the difficulty:

—	Ages	Population	Deaths	Death-rate
Year A	0–40	400,000	8	2
	40–	200,000	100	50
	All ages	600,000	108	18
Year B	0–40	200,000	3	1·5
	40–	400,000	160	40
	All ages	600,000	163	27

* From the Milroy lectures for 1959, delivered before the Royal College of Physicians of London on Feb. 3 and 5.

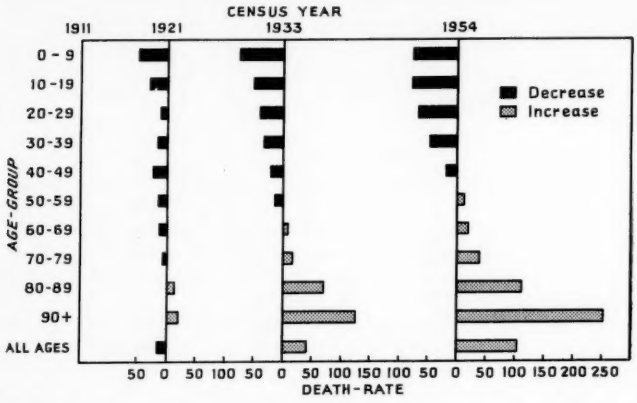


Fig. 9—Using the rates for 1911 as the standard, changes are shown in death-rates for cardiovascular-renal diseases in ten-year age-groups for recent census years.

Ischæmic Heart-disease

A century ago Stokes said that the key to understanding disease of the heart is to know the state of the heart muscle (Stokes 1854), and Mackenzie never tired of stressing that point. Allan Burns (1781–1813), of Glasgow, had long previously produced experimental evidence (based on the effects of ligating the arteries of limbs) that angina pectoris was the result of myocardial ischæmia (Willius and Dry 1948). From the work of J. B. Herrick (1912) the dramatic effects of sudden obstruction of the coronary arteries became widely known, although Leyden in 1884 had described the condition (Willius and Dry 1948).

Three conditions or stages may be noted: (1) early atherosclerosis of the coronary arteries without appreciable narrowing or occlusion and generally without symptoms, (2) atherosclerosis with coronary narrowing, characterised by attacks of angina pectoris, and (3) coronary occlusion with myocardial infarction (coronary-artery thrombosis). The clinical features are not always clear cut; for instance, a subacute state is sometimes described, with clinical features between those of angina pectoris and myocardial infarction—the intermediate coronary syndrome. That condition may arise from the occluding lesion in an arterial branch gradually becoming complete, or from thrombosis in a small branch; in general, the term is best avoided—or, if retained, used as a temporary resting-place pending firm diagnosis.

What is the nature of this arterial disease that gives us so much concern today? Turnbull's definition (1915) of atheroma was "a degeneration which affects, and is almost confined to the intima. . . . The degeneration is characterised by the accumulation of debris which is at first fatty and is later impregnated by calcium." The fatty substance consists mainly of cholesterol and its esters. Commonly the lesions are widespread and irregular in distribution. They are important because they narrow the lumen of the vessels affected, and because complete obstruction at the site may suddenly occur from thrombosis: the symptoms angina pectoris and intermittent claudication, and the lesions of limb gangrene, myocardial infarction, and cerebral thrombosis all have in ischæmia their common origin.

Atherosclerosis (W.H.O. 1957a) includes several quite distinct intimal processes—fatty changes, fibrous thickening, fibrin incorporation, and calcification. The cause or causes of those changes is still being keenly sought. There are two main hypotheses. The first is that the intimal plaques represent a reaction, in which lipid infiltration is an important feature, to some primary change in the arterial wall. The primary change has been attributed variously: Rokitansky and later Duguid blamed a mural thrombosis, Winternitz thought it to be an intramural hæmorrhage, and Virchow called it a necrobiosis. The second hypothesis is that atherosclerosis presents the local effects of a generalised disturbance of lipid metabolism.

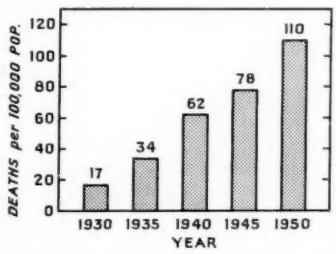


Fig. 11—Death-rates in Australia per 100,000 population are shown for selected years for diseases of the coronary arteries and *angina pectoris*. The rapid increase is similarly noted in England and Wales, Canada, United States of America, New Zealand, and many other countries.

Morris and Crawford (1958) present evidence "dissociating ischæmic heart disease from coronary artery disease. . . . There is good reason to believe that the former has increased during this century; the latter may have declined in Britain during the past 40 years." They suggest that regular physical exercise may promote cardiovascular health in middle age, and that "ischæmic heart disease may be in some degree a deprivation syndrome, a deficiency disease".

From a series of 6850 postmortem examinations made in Adelaide, Cleland (1949) reported 147 cases of cardiac infarction; he noted an increase from 11 cases per 1000 examinations in 1920–25 to 45 per 1000 in 1946–47. Most deaths in the series occurred in the 7th decade, and there were twice as many males as females. He thought that atheroma

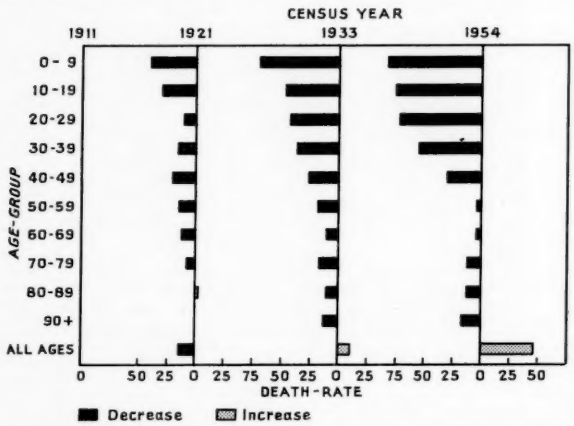


Fig. 10—As in fig. 9, changes in death-rates are shown for the combined group C.V.R. plus "senility" and "ill-defined" causes. An interesting feature is that a decrease has occurred in every ten-year age-group, although the rate for all ages combined has increased by 50% (vide footnote).

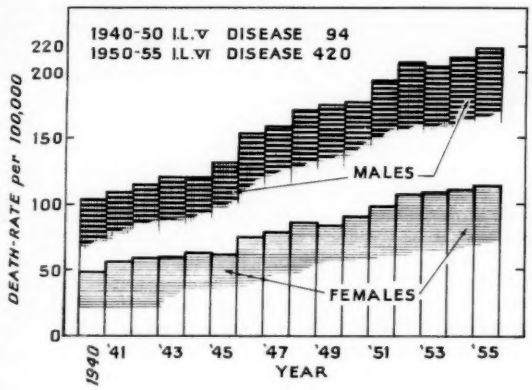


Fig. 12—The steady increase year by year from 1940 to 1955 in the death-rates for coronary-artery disease in Australia is shown for each sex, using the International List classifications indicated. For the years 1940-50 code no. 94 of Fifth Revision is used; for 1950-55 code no. 420 of the Sixth Revision.

had declined in incidence in recent years, but that coronary thrombosis had increased.

Evans (1956) reports that in 60% of cases of cardiac infarction, in a series studied, no evidence of coronary thrombosis was found post mortem; but there was coronary atherosclerosis (apparently with occlusion) in 90% of the cases.

Coronary atherosclerosis and coronary thrombosis—are they, in fact, two separate diseases? We do not regard diabetic coma as a disease distinct from diabetes mellitus, but rather as a complication of it. It is certainly a condition requiring special preventive and curative treatment—but still a complication. So we may properly think of coronary thrombosis as a grave complication of coronary atherosclerosis, demanding special attention. And it appears that thrombosis is prone to occur in certain groups of atherosclerotic subjects; diabetic coma also has its predilection—it is a more likely hazard in young diabetics than in the elderly.

But still the question "Why atheroma?" awaits satisfactory answer; and—even given the atheromatous lesion—a satisfying answer to the other question "Why thrombosis?" is also elusive. Can biochemistry supply the answers?

The Arraignment of the Fats

It is recorded (*Leviticus* VII, 24) that the Lord instructed Moses to tell the children of Israel to eat no manner of fat. Nor at the turn of the present century did nutritionists hold the fats in very high regard, except for their calorific value; and even as energy-producers their place could be just as well taken by a commensurate calorific allowance of proteins or carbohydrates. It was agreed, of course, that a suitable amount of fatty food gave pleasant comfort to the digestive organs, especially in quickly relieving the pangs of hunger: the satiety-value of fats is high. And, anyway, most of us "do like a little bit of butter" on our bread.

Then came the day of Gowland Hopkins and the discovery of vitamins. The fact that some fats were vitamin-carriers gave them better status. Indeed certain fats, constituted with unsaturated fatty acids, were regarded by some biochemists as being themselves vitamins. Those acids were called "essential fatty acids" (vitamin F). Burr and Burr (1930) showed that rats suffered if their diet did not include the nutritionally essential, unsaturated fatty acids—linoleic, linolenic, and arachidonic. How important those acids are in human nutrition is uncertain. They have some unsaturated carbon atoms, and so one or more double bonds, which can be abolished by the addition of oxygen, hydrogen, or a halogen. Unsaturated fats can be converted by hydrogenation into completely saturated fats. This "hardening of fats" is useful technically (in making margarine, for instance, from vegetable oils), but nutritionally the change may not be wholly advantageous.

The biochemical approach to atherosclerosis involves consideration especially of the lipids. First the steroid cholesterol was blamed. Cholesterol and cholesterol esters being the main constituents of atheromatous plaques, it was natural to think that a high cholesterol content of the diet might initiate or at least facilitate the development of the lesions. Even now the precise function of cholesterol in human metabolism is undetermined—but the biochemistry of steroids generally and their metabolism are being actively studied. Experimental feeding of rabbits on diets rich in cholesterol was found to produce deposition of it in the arterial intima, and a condition resembling atheroma. Further studies brought fats in general into the limelight—and there they still are.

Researches into the cholesterol-fat problem in atherosclerosis have gone on so rapidly and so profoundly that a clinician, inadequately versed in biochemistry, hesitates to proffer opinions. The discussions have become so vigorous that an intending participant needs, besides biochemical knowledge, some expertness in semantics and skill in polemics. I fear I am throwing discretion to the winds in here setting out the current views, as a series of brief, even terse, statements:

1. A group association exists between the incidence of atherosclerosis in human subjects and a high level of cholesterolæmia.

2. Rabbits on cholesterol-rich diets develop lesions in their arterial walls (Anitschkow, in Cowdry 1933). A large volume of useful work on experimental atherosclerosis has been done (e.g., Katz and Stamler 1953). To reduce the dietary intake of cholesterol does not necessarily lower the concentration of it in the blood. James (1958) has noted that the reduction in the diet is followed by increased synthesis of cholesterol by the liver.

3. In man, high-fat diets in general induce high cholesterolæmia. Low-fat diets reduce the level, but the continued taking of such low diets is "biologically unsound" (Kinsell et al. 1958). There are anomalies: some people get hyperlipæmia from a low-fat diet, especially if the carbohydrate intake is high.

4. The nature of the fats may be a more potent factor than their quantity. Diets rich in animal fats commonly raise the cholesterol level; and those with much vegetable fat usually depress it (Kinsell et al. 1958, Bronte-Stewart et al. 1956), and so do marine oils (Ahrens et al. 1959).

5. Sinclair (1958) contends that atherosclerosis comes from taking diets low in essential fatty acids. Vegetable fats generally have a high content of linoleic and other unsaturated fats. Ahrens thinks the lowering of serum-lipids when they are taken is not a function of their essentiality but of their unsaturation.

6. Several investigators claim that a high ratio of saturated to unsaturated fats in the diet is the significant factor (e.g., Malmros and Wigand 1957).

7. Persons with familial or essential hyperlipæmia are prone to develop atherosclerosis at an early age (Thanhauser 1950).

8. Recent biochemical studies have added extensively to knowledge of lipid metabolism, especially on the transport

and utilisation (Baldwin 1948), both features likely to be involved in atherosclerosis.

9. Most of the lipid substances in the blood are attached to globulin, the combination being the lipoproteins. Those complexes show a wide range of composition, from a fat percentage as high as 98 (as in the chylomicrons) to as low as 1 (albumin/fatty acid); α and β lipoproteins lie between these extremes. Compared with the α form, β-lipoproteins in the plasma are increased in patients with myocardial infarction (Barr 1953) and generally in those with advanced atherosclerosis (Smith 1957). Smith cites pre-β forms as significant.

10. Hartroft and Thomas (1957) produced myocardial infarcts in rats by feeding them on diets rich in saturated fats. I am not aware of earlier experiments with that successful result. It is established that high-fat diets not only favour the development of atherosclerosis but also the occurrence of its direst complication.

Attempts to evolve a biochemical test as an " atherogenic index " have so far failed. Much was hoped from the vast study made in the United States two years ago to evaluate measurements of serum lipoproteins and of cholesterol as predictors of clinical complications of atherosclerosis (National Advisory Heart Council 1956). The result was disappointing. The findings gave no basis for a clinical predictive test beyond a range of group probability.

The experimental work of Hartroft and Thomas gave results in conformity with the studies of Fullerton and colleagues (1953), who showed that high lipid concentration in the blood facilitates the clotting process; McDonald and Fullerton (1958) found that exercise reduced that effect. High intake of fat by human subjects may encourage the development of thrombosis in diseased arteries, though a recent report by O'Brien (1958) raises doubts.

What we eat certainly appears influential in the ætiology of atherosclerosis. The fat content of the diet and the total calorific value are suspect; the kind of fat rather than the amount of fat may be important. It would seem, too, that a high intake of carbohydrate food can be important; excess over immediate metabolic need is converted to fats for storage and subsequent catabolic breakdown. Kinsell found that a high-carbohydrate diet raised the serum-cholesterol, and that substituting polyunsaturated fats for the carbohydrate lowered the cholesterol level.

In short, in the matter of atherosclerosis and myocardial infarction, the accused, " Fat-in-the-diet ", stands charged. It is suspected as *particeps criminis* in the cause of atherosclerosis, and perhaps also in that of thrombosis: it may, as it were, be an accessory both before and after the fact of coronary-artery disease. The case stands part heard, pending the calling of further evidence.

Racial Differences

Many investigators have shown the varying incidence of atherosclerosis in different ethnic groups. In the Australian aborigines low serum-cholesterol levels and a low incidence of atheroma contrast with those in the white Australian population (Schwartz and Casley-Smith 1958). The aborigines also show lower blood-pressure levels (Casley-Smith 1958). The natives of New Guinea are reported to have a low incidence of coronary heart-disease and related vascular disorders. De Wolfe and Whyte (1958) found that, whereas white Australians derive about 40% of their total calorific intake from fat, the natives of New Guinea get only about 5% in that way. Like Australian aborigines, New Guinea natives showed no upward trend of serum-cholesterol level with age, and the value was generally lower in males than females.

Mann et al. (1955) reported similar conditions in Nigerian natives. The work of Bronte-Stewart with Bantu natives in South Africa is well known. Similar reports have been made on numerous other groups, including Italians, Navajo Indians, and Eskimos. The question is whether the differences observed arise from differences of race or of habits of living. Interesting studies were made of three sets of Japanese (Larsen 1957, Keys et al. 1958): (1) people living in Japan, (2) Japanese who had lived many years in Hawaii, and (3) some long settled in California. The lipid levels in the blood were highest in the Californian group and lowest in those resident in Japan. Keys investigated especially the differences in diets, and said that the amount of arterial change was proportionate to the fat intake.

Studies of various people—in Australia, New Guinea, Japan, and elsewhere—support the view that racial differences have little or no influence on the incidence of atherosclerosis. Environment (in the broadest sense, including the diet) is of more significance. We appear all to be brothers under the skin.

The Effect of Ageing

The poet lauds " . . . the land of faery,
Where nobody gets old . . . "

The serum-cholesterol level usually rises with age, and the high incidence of atherosclerosis in older people has been related to that fact. But atherosclerosis seems not to be inevitable with ageing; Morgagni reported on the necropsy of a woman of 90 with very little arterial damage (Cowdry 1933). It has been suggested, too, that the aged are better able to withstand coronary occlusion than middle-aged subjects; by injecting coronary arteries of hearts from persons of various age-groups with radio-opaque fluid, Gross found that the collateral circulation of the coronary system improved with advancing years. Victims of severe circulatory episodes, such as attacks of acute pulmonary œdema, may live sometimes for ten or even twenty years, with excellent capacity for work. " This can happen only when physician and patient refuse to accept the idea that ageing of the heart (presbycardia) is a relentlessly progressive disorder " (Dock 1956).

The biology of ageing has been much studied in recent years, and some investigators regard the bodily changes (even to death) commonly associated with old age as a kind of accidental phase.

" If we view ' natural death ' as the termination of existence due to the uniform senescent atrophy of all the structures of the organism, leading to uniform depression and ultimately simultaneous extinction of all its functions, then ' natural death ' in all probability never occurs. In a world in which the organism could be completely shielded from fortuitous strains and the invasive activities of parasitic organisms, the phenomenon of natural death might conceivably occur. In actuality death is always in some measure accidental." (Robertson 1923.)

But are there not " normal " degenerative effects of old age? Can the ageing tissues escape the effects of wear and tear?

Many clear reports (e.g., Gertler and White 1954, Moon 1957) have been made on the occurrence of atherosclerosis in young adults. Arterial changes, uncomplicated by hypertension, xanthomatosis, diabetes, or nephrosis have commonly been found in men under the age of 40 dying from accident or other causes. There have been

reports of " degenerative " changes in coronary arteries in the bodies of infants, with deposition of lipid droplets; in some older children there were gross changes of atherosclerosis (Prior and Jones 1952). Circumstances associated with the clinical condition of progeria are apposite; victims of that condition of premature senility usually present signs of gross atherosclerosis in childhood and die of coronary thrombosis.

Osler regarded arteriosclerosis as an " involution process. "

" Longevity is a vascular question. . . . The onset of what may be called physiological arteriosclerosis depends in the first place upon the quality of arterial tissue (vital rubber) which the individual has inherited and secondarily upon the amount of wear and tear to which he has subjected it."

Aschoff (as Lansing later) distinguished the age changes in arteries from those of atherosclerosis:

" Hardening and thickening of the vessels (senile fibrosis) occur from ageing but the walls stretch and become tortuous, and the lumina are not narrowed. . . . Ageing alone never causes the deformations of the vascular wall typical of arteriosclerosis, which is a disease of the vessels manifesting itself in senescence." (Cowdry 1933).

Whatever the causes of atherosclerosis, the length of time they operate is surely a highly significant factor. Atherosclerosis comes especially in old age, but is not its inevitable accompaniment. The disease may occur in children. It is noted, too, that fatal coronary attacks appear commoner in men of 50 to 60 than in older people. The condition of a man's arteries is not only the criterion of his age but also the determinant of his longevity. Not all old people show an advanced degree of atherosclerosis, but most do; in the majority of those the disorder is the main cause of death.

Some Other Suspected Factors

Other factors besides the fats of the diet, the racial type, and senescence have been blamed for causing atherosclerosis.

Heredity has commonly been suspected. Studies of identical twins may be expected to provide useful data, but not enough have yet been done. High familial incidence has often been reported (Thomas and Hischorn 1955).

Sex is a factor. Atherosclerosis and its effects are more commonly seen in men than women; deaths from coronary-artery disease in Australia show a male/female ratio of 2/1 (fig. 12). In the 6th decade of life the ratio is about 4/1; in the 7th and subsequent decades the incidence of arterial changes in females approaches that found in elderly males.

Occupation has been much discussed. Ryle and Russell (1949) and Morris (1957, 1958) consider it a potent factor. Active routine jobs requiring physical exertion seem least hazardous. Morris and Crawford (1958), in their illuminating and painstaking work, found that " the hearts of sedentary and light workers showed the pathology of hearts of heavy workers 10–15 years older ". Nobody appears yet to have suggested " Be a bus conductor and keep your heart young " as a clarion call for use of the London Transport Board when looking for staff.

Atherosclerosis is said to be more frequently found in persons of mesomorphic body-build. Obesity has been blamed: Wilens (1947) found that severe atheroma was ten times as frequent in obese people as in lean subjects of similar age.

Food factors other than the fats have been suspected. Overnutrition (McCance 1953) and a general luxus dietary (Keen and Rose 1958) seem potent: further study of the metabolism of plethora is likely to be illuminating. Overfeeding of babies may render them prematurely liable to atherosclerosis; it appears that improved nutrition shortens the period of childhood and promotes early maturation (Comfort 1956); it may lead to shortening of the life-span. Over-demanding babies, beware! Best found that animals on a choline-deficient diet were especially prone to atherosclerosis; but it is doubtful whether that finding can be extrapolated to the problem in human subjects (Best 1956).

Smoking has also been placed in the dock. Osler in 1910 expected " an increasing number of cases of . . . angina in women, with the rapid increase of cigarette smoking ". Henderson, using the ballistocardiogram, found that the effect of smoking a single cigarette could be noted in persons who had evidence of coronary heart-disease: healthy young people showed no effect. Studies of Doll and Hill (1956) have also shown the possible influence of smoking: in the groups studied the incidence of atherosclerosis was 42% higher in heavy smokers. Brown et al. (1957) think smoking has no such ill effects in old men over 70.

Emotional stress, of course, has long been suspected. Ischlondsky (1952) has reported his studies on the effects of the emotions, and the work of Wolf et al. (1955) is noteworthy. Morris discounts the influence of emotional stress on the incidence of coronary heart-disease.

The endocrines have been called to account. Oliver and Boyd (1956), while accepting the view that a disorder of fat metabolism is a causative factor, blame also " an individual susceptibility which is not well understood, but is probably partly determined by heredity and by endocrine factors ".

Magarey (1956) is one who thinks that the stress of raised blood-pressure on the arterial walls is a prime factor in atherosclerosis. Texon's studies on hæmodynamics support that view (Texon 1957). The disturbing influence of cardiac hypertrophy on the coronary circulation may be significant.

Toxic agents such as lead play little part now, for preventive measures are effective; alcohol is not usually blamed—indeed its use as a vasodilator has been advised.

It is common to exculpate the infections, but I think that may be rash. Chronic infections of the biliary tract are often associated with coronary heart-disease. We have little knowledge of possible chronic damage from infections in general; the vascular wear and tear associated with severe infections, especially those with long-lasting fever, may be considerable. It has been said, on the other hand, that the metabolic disturbance or perhaps the low dietary in debilitating illnesses reduces the atherosclerotic tendency. There is no doubt that infections in the elderly are serious affairs: a respiratory infection, even the common cold, with its associated stresses of toxins, fever, and coughing, may be the " last straw " for a circulatory system near the breaking-point.

" Pathogenic Situations "

Many factors, then, are under suspicion, but knowledge of the real cause of atherosclerosis still eludes us. It may come from the combined operation of several factors. It certainly is no clear-cut matter—in the way that tuberculosis comes from infection by the bacillus—and even

that is not as simple as we once thought. The current view is that atherosclerosis is not merely an effect of ageing, but that it is a disease—a disease in which altered cholesterol-lipid-lipoprotein metabolism plays an essential part. Lifelong addiction to a high-fat dietary seems a potent factor. Of people so addicted, some become victims of the disease; the interplay of several other factors—physical activity, heredity, sex, hormones, hypertension, stress—is generally involved. That, in short, appears to be the generally accepted view at the present time.

Morgan (1956) has presented an excellent review of that doctrine of multiple causes as it bears on atherosclerosis. It has wider application. We may not accept all of Selye's ideas, but we can agree with him in this: ". . . there begins to emerge a new and somewhat more complex pathology, in which the main objects of our study are no longer individual pathogens, but rather pathogenic situations" (Selye 1952). That notion is fundamental in our study of atherosclerosis.

Bases for Action

Though the use of modern methods of investigation, in institutions replete with elaborate apparatus operated by highly trained technicians, is producing a wealth of data, cardiological research is not merely a matter for laboratories, nor is the specialist in his consulting-room, even with the array of apparatus, in the best position to supply some types of information. Large epidemiological surveys, continued over many years, as those at Framingham and Albany in the United States, are likely to help. Small groups are not to be neglected, and many of the problems in cardiovascular diseases are best studied by the alert general practitioner. Pickles has shown how the doctor in the country can solve some of the problems in infectious disease, and the same type of study can well be applied to cardiovascular disease. Long-term observation of small groups of people in a stable community may supply many missing bricks in the structure of knowledge we are trying to build. Sometimes the physician may usefully study himself, for he is a high-risk subject.

The continuity of care provided by the general practitioner enables him to study the health and the illnesses of his patients, and that work is essential to progress in medicine—no less now than it was when Mackenzie (Wilson 1926) eulogised it fifty years ago. But for research studies in clinical practice to be of value, as for any research, it is fundamentally important that their planning be careful and their recording orderly. The inquiries being developed by the College of General Practitioners in Britain have great possibilities; the sister college in Australia is taking up similar work.

Public-health departments now give much attention to health education. We try to tell the public the truth—when we know what it is. What can we say of atherosclerotic heart-disease? The information and advice suitable for individual patients may be adapted to mass needs, and based on such facts as these:

1. The outlook for controlling heart-disease is not without hope. Modern knowledge has enabled some forms, till recently formidable in their effects, to be controlled. Some other forms—though not yet preventable—can be detected in their early stages, and are amenable to treatment.

2. The main form of heart-disease remaining resistant to control is that associated with the wearing-out of the blood-vessels, especially atherosclerosis.

3. In the populations of most countries the proportion of elderly people is increasing; doctors and statesmen are giving more thought to geriatrics.

4. Atherosclerosis is pre-eminently a disease afflicting old people, and is present in some degree in almost everybody past middle life.

5. High blood-pressure is also a prevalent disorder, but may be compatible with long years of active life. Its ultimate effects are similar to those of atherosclerosis, of which condition high pressure may be a causal factor.

6. The precise cause of atherosclerosis is obscure. Many factors seem involved, and some of them can be removed or reduced. The dangerous complication, coronary thrombosis, may be rendered less likely by taking suitable care.

7. Overeating in general, but especially an excess of animal fats, favours the development of atherosclerosis, and probably of its thrombotic complication. Complete abstention from fats is, of course, impracticable. Indeed, nutritionists today hold the fatty acids to be the main fuel of the body.

8. Smoking, emotional stress, and a "high pressure" way of life are suspected to be factors. The cultivation of hobbies and of wide interests probably favours longevity.

9. For well people and for "heart cases", physical activity, within the range of their comfortable capacity, is desirable. Hard work, done with discretion, assists the coronary circulation. The judicious mixture of rest and exercise (the principle of Buerger's exercises) is desirable.

10. Arterial degeneration appears almost an integral feature of ageing and wearing out. Father Time will not be thwarted—but his activities may be postponed.

It may seem that in such a decalogue we are only advising as Ovid of old did: "*medio tutissimus ibis*", or as the *regimen sanitatis* of the Salerno school of the Middle Ages: "... gainst all surfets vertues schoole hath taught to make the gift of temperance a shield." That seems trite, yet we can hardly with confidence go further.

For atherosclerotic heart-disease there is no way of discovering in advance who will be a victim, or when the disease will strike: one who has given a normal electrocardiographic tracing today may have a fatal coronary attack tomorrow—or even today, perhaps ten minutes after the test. Nor, even if we were able to discern over whom the damoclean sword is hanging, could we do anything to avert its fall; we could only ply him promptly with anticoagulants and sedatives in the hope of minimising the effects of the blow.

Developments in the teaching of public health in this century reflect a changed outlook on the subject. From being a set of studies on environmental sanitation it has now made firm links with clinical medicine. For example, in our Adelaide medical school, Dr. Frank Hone, a physician of vision and understanding, introduced that concept thirty years ago, and it was elaborated by him and by myself. The application of preventive measures in cardiological practice has been used for students as an illustration of method, for it is impracticable and unnecessary to present to them a comprehensive and detailed preventive programme for every kind of illness. If they are given the preventive outlook and shown how to use it in practice for one group of diseases, some progress has been made. The standard of medical practice of the future depends on the students' training now.

Many friends have given me generous help—in this country particularly Sir Allen Daley and Dr. W. P. D. Logan and Dr. J. N. Morris; in North America Prof. E. Gurney Clark, Prof. Hugh Leavell, Prof. Neil McKinnon, Prof. D. D. Rutstein, Dr. H. E. Hilleboe, Dr. Richard Lee, Dr. G. V. Mann, Dr. P. D. White, and

Miss Marjorie Bellows and other officers of the American Heart Association; in Australia Prof. H. N. Robson, Prof. F. R. Magarey, Dr. H. R. Marston, F.R.S., Dr. D. E. Dunn, Mr. A. W. Bowden and Mr. H. L. Semmens (of the Government Statist's Department), Miss D. Mead (of the medical library in the University of Adelaide), and Mrs. Joan Strudwick and Mr. B. J. Plew (of the South Australian Department of Public Health). I am very grateful to them all.

REFEFENCES

Ahrens, E. H., Jr., and colleagues (1959) *Lancet*, i, 115.
Baldwin, E. (1948) Dynamic Aspects of Biochemistry. London.
Baron, J. (1838) Life of Edward Jenner. London.
Barr, D. P. (1953) *Circulation*, **8**, 641.
Best, C. H. (1956) *Proc. roy. Soc. B*, **145**, 157.
Bronte-Stewart, B., Antonis, A., Eales, L., Buck, J. F. (1956) *Lancet*, i, 521.
Brown, R. G., Davidson, L. A. G., McKeown, T., Whitfield, A. G. W. (1957) *ibid.* ii, 1073.
Burr, G. O., Burr, M. M. (1930) *J. biol. Chem.* **86**, 587.
Byrom, F. B. (1954) *Lancet*, ii, 202.
Carter, A. H. (1896) *Brit. med. J.* i, 1296.
Casley-Smith, J. (1958) *Aust. J. exp. Biol. med. Sci.* (in the press).
Cleland, J. B. (1949) *Med. J. Aust.* ii, 733.
Coburn, A. F. (1931) The Factor of Infection in the Rheumatic State. Baltimore.
Comfort, A. (1956) The Biology of Senescence. London.
Cowdry, E. V. (1933) Arteriosclerosis. New York.
De Wolfe, M. S., Whyte, H. M. (1958) *Aust. Ann. Med.* **7**, 47.
Dock, W. (1956) *Bull. N.Y. Acad. Med.* **32**, 175.
Doll, R., Hill, A. B. (1956) *Brit. med. J.* ii, 1071.
Evans, W. (1956) Cardiology. London.
Fullerton, H. W., Davie, W. J. A., Anastasopoulos, C. T. (1953) *ibid.* ii, 250.
Gertler, M. M., White, P. D. (1954) Coronary Heart Disease in Young Adults. Boston.
Gregg, N. (1941) *Trans. ophthal. Soc. Aust.* **3**, 35.
Hartroft, W. S., Thomas, W. A. (1957) *J. Amer. med. Ass.* **164**, 1903.
Herrick, J. B. (1912) *ibid.*, **59**, 2015.
Holmes, M. C., Williams, R. E. O. (1958) *J. Hyg., Camb.* **56**, 43, 62.
Illingworth, R. S. (1958) *Lancet*, ii, 653.
Ingalls, T. H. (1956) *J. Amer. med. Ass.* **161**, 1047.
Ischlondsky, N. E. (1952) Brain Mechanisms in Coronary Disease. London.
James, A. T. (1958) *in* Chemistry of Lipides as related to Atherosclerosis (edited by I. H. Page). Springfield, Ill.
Katz, L. N., Stamler, J. (1953) Experimental Atherosclerosis. Springfield, Ill.
Keen, H., Rose, G. A. (1958) *Brit. med. J.* i, 1508.
Kellner, A. (1956) *Bull. N.Y. Acad. Med.* **32**, 534.
Keys, A., Anderson, J. T., Grande, F. (1958) *Lancet*, ii, 959.
Kinsell, L. W., Michaels, G. D., Friskey, R. W., Splitter, S. (1958) *ibid.* i, 334.
Lancaster, H. O. (1957) *Med. J. Aust.* ii, 821.
Lansing, A. I. (1956) *Bull. N.Y. Acad. Med.* **32**, 5.
Larsen, N. P. (1957) *Arch. intern. Med.* **100**, 436.
LeFanu, W. R. (1951) A Bio-bibliography of Edward Jenner. London.
Lew, E. A. (1957) *J. chron. Dis.* **6**, 192.
Lewis, T. (1942) Diseases of the Heart. London.
Magarey, F. R. (1956) *Med. J. Aust.* ii, 473.
Malmros, H., Wigand, G. (1957) *Lancet*, ii, 1.
Mann, G. V., Nicol, B. M., Stare, F. J. (1955) *Brit. med. J.* ii, 1008.
Mantle, A. (1885) *ibid.* ii, 960.
McCance, R. A. (1953) *Lancet*, ii, 685.
McDonald, G. A., Fullerton, H. W. (1958) *ibid.* i, 598.
Medical Research Council (1927) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 114.
— (1955) *Brit. med. J.* i, 555.
Miller, D., Garvan, J. (1957) *Brit. J. Surg.* **44**, 396.
Moon, H. D. (1957) *Circulation*, **16**, 263.
Morgan, A. D. (1956) The Pathogenesis of Coronary Occlusion. Oxford.
Morris, J. N. (1957) Uses of Epidemiology. London.
— (1958) *Circulation*, **17**, 321.
— Crawford, M. D. (1958) *Brit. med. J.* ii, 1485.
National Advisory Heart Council (1956) *Circulation*, **14**, 691.
Newsholme, A. (1895) *Lancet*, i, 589, 657.
O'Brien, J. R. (1958) *ibid.* i, 410.
Oliver, M. F., Boyd, G. S. (1956) *ibid.* ii, 1273.
Osler, W. (1913) The Principles and Practice of Medicine. London.
Pickering, G. W. (1955) High Blood Pressure. London.
Platt, R. (1947) *Quart. J. med.* **16**, 111.
Prior, J. T., Jones, D. B. (1952) *Amer. J. Path.* **28**, 937.
Robertson, T. B. (1923) The Chemical Basis of Growth and Senescence. Philadelphia.
Royal College of Physicians (1957) Further Report of Rheumatic Fever Committee.
Ryle, J. A., Russell, W. T. (1949) *Brit. Heart J.* **11**, 370.
Sangster, C. B. (1940) *Med. J. Aust.* i, 461.
Schlesinger, B. E. (1955) *Practitioner*, **175**, 563.
Schwartz, C. J., Casley-Smith, J. R. (1958) *Aust. J. exp. Biol. med. Sci.* **36**, 117.
Selye, H. (1952) The Story of the Adaptation Syndrome. Montreal.
Sheldon, W. (1958) *Med. Annu.* p. 40.
Sinclair, H. M. (1958) *Lancet*, i, 639.
Smith, E. B. (1957) *ibid.* ii, 910.
Smith, P. K., McMichael, J., Murphy, E. A. (1958) *Quart. J. med.* **27**, 117.
Stocks, P. (1950) *Brit. med. J.* i, 56.
Stokes, W. (1854) Diseases of the Heart and Aorta. Dublin.
Texon, M. (1957) *Arch. intern. Med.* **99**, 418.
Thanhauser, S. J. (1950) Lipidoses. London.
Thomas, C. B., Hischorn, B. (1955) *Ann. intern. Med.* **42**, 90.
Todd, E. W., Coburn, A. F., Hill, A. B. (1939) *Lancet*, ii, 1213.
Turnbull, H. M. (1915) *Quart. J. med.* **8**, 201.
Wilens, S. L. (1947) *Arch. intern. Med.* **79**, 129.
Willius, F. A., Dry, T. J. (1948) A History of the Heart and the Circulation. Philadelphia.
Wilson, R. McN. (1926) The Beloved Physician. London.
Wolf, S., Cardon, P. V., Shepard, E. M., Wolff, H. G. (1955) Life Stress and Essential Hypertension. Baltimore.
World Health Organisation (1957a) Technical Report Series, no. 117.
— (1957b) *ibid.* no. 126.
Yerushalmy, J., Hilleboe, H. E. (1957) *N.Y. St. J. Med.* **57**, 2343.

SUPPRESSION BY CORTISOL OF INCREASED SERUM-TRANSAMINASE INDUCED BY ENDOTOXIN

JAMES C. MELBY
M.D. Minnesota
INSTRUCTOR IN MEDICINE

RICHARD H. EGDAHL*
M.D., Ph.D. Minnesota
ASSOCIATE SCIENTIST (SURGERY)

IRENE C. BOSSENMAIER
B.A. Minnesota
ASSISTANT SCIENTIST (MEDICINE)

WESLEY W. SPINK
M.D. Minnesota
PROFESSOR OF MEDICINE

From the Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota

SHOCK due to infection by gram-negative bacteria is presumably related to the liberation into the blood-stream of endotoxin from the bacteria (Weil and Spink 1958, Hall and Gold 1955, Waisbren 1951). Bacterial endotoxins have also been implicated in the development of irreversible shock associated with hæmorrhage and trauma (Mansberger et al. 1958, Jacob et al. 1954). Protection against the lethal effect of bacterial endotoxin by pre-treatment with cortisol (hydrocortisone) or its analogues has been demonstrated in various mammalian species (Spink and Anderson 1954, Thomas 1958, Halberg et al. 1956). This protection was accomplished by doses of steroid hormones far in excess of the amount the particular laboratory animal could produce endogeneously. Secretory failure of the adrenal glands has not been demonstrated in the dog after lethal doses of endotoxin, nor in man with circulatory collapse due to infection (Melby et al. 1957, Melby and Spink 1958). The beneficial effects of cortisol in ameliorating or preventing the toxicity of brucella endotoxin in man are additional evidence for the repeated observations that steroids are helpful in the treatment of shock due to infection in which endotoxin contributes to the prostration (Abernathy and Spink 1958, Spink 1957, Spink and Hall 1952). Thus the beneficial effect of the steroids provides evidence, not of adrenal insufficiency, but rather of a pharmacological action.

The mechanism by which cortisol protects against endotoxin is unknown. A single injection of a large dose of endotoxin into mature laboratory animals regularly results in fever, shock, and death (Halberg et al. 1956). Weil et al. (1956) have shown that an intravenous injection of endotoxin is followed by a predictable and reproducible characteristic sequence of events with pooling of a significant proportion of the blood-volume in the splanchnic vessels and resultant reduction in cardiac output. Pathologically, there was widespread hæmorrhagic necrosis of the mucosa of the gastrointestinal tract and subendocardial area of the heart.

Measurement of the serum-glutamic-oxalacetic-transaminase (S.G.O.T.) activity provides a sensitive but non-specific index of cellular injury or change in cell-membrane permeability of tissues which have a high intracellular content of this enzyme under normal conditions—including cardiac and skeletal muscle and renal and hepatic tissues (Wroblewski 1956). Watson (1957) found a rise in S.G.O.T. activity in rabbits following intravenous injections of streptococcal toxin. Similar observations have been made in monkeys following the feeding of staphylococcal enterotoxin (Sugiyama et al. 1958). In the experiments reported here the level of S.G.O.T. activity as an index of cellular injury was studied to determine:

* Present address: Department of Surgery, Medical College of Virginia, Richmond, Virginia.

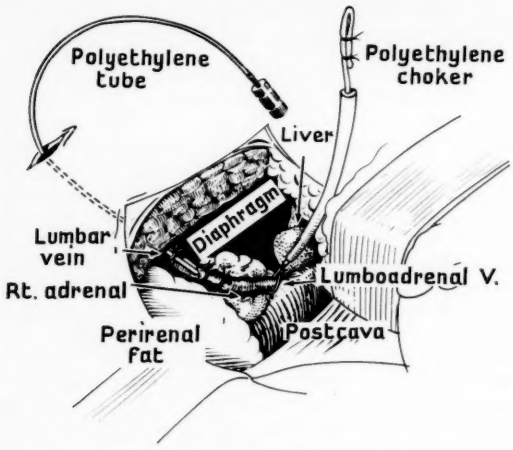


Fig. 1—Position of the Hume-Nelson adrenal-vein cannula.

(1) the degree of injury produced by endotoxin, (2) the effectiveness of exogenous cortisol in preventing cellular injury by endotoxin, and (3) the significance of endogenous cortisol production in the protection against injury by endotoxin.

Materials and Methods

39 adult mongrel dogs ranging from 6 to 23·7 kg. in weight were used. All of the animals were anæsthetised with pentobarbitone sodium (30 mg. per kg.) before being subjected to experimental procedures. A permanent polyethylene cannula was placed in the right lumboadreanal vein of 11 of the dogs according to a technique described by Hume and Nelson (1955) (figs. 1 and 2). This preparation permits either continuous or intermittent collection of the total venous effluent of the right adrenal gland. Using this cannula technique, adrenal venous blood was collected for periods of five minutes at varying intervals, following which the cannula was filled with 4% heparin in physiological saline solution. Peripheral-blood specimens were obtained from the femoral vein by means of a small-gauge polyethylene catheter. Blood specimens were analysed for cortisol by a modification of the method of Silber and Porter (1954) as described by Peterson et al. (1957). This

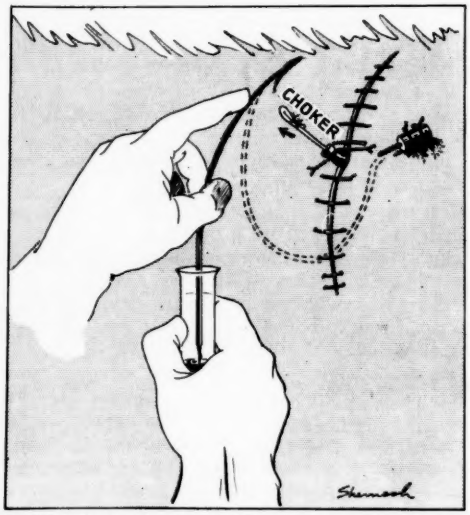


Fig. 2—Method of collection of total adrenal venous effluent with the Hume-Nelson cannula.

method is specific for steroids with the 17,21-dihydroxy-20-keto configuration including cortisol, cortisone, 11-deoxycortisol, and their dihydro- and tetrahydro-derivatives. Of these, only cortisol exists in the plasma in significant concentrations; therefore, the method may be regarded as highly specific for cortisol, the principal adrenal secretory product in the dog (Farrell 1954). Peripheral-blood specimens were used in the determination of S.G.O.T. activity by the method of Karmen et al. (1955).

Purified endotoxin of the Boivin type derived from *Escherichia coli* and prepared by the method of Spink and Anderson (1954) was used in a dosage of 1·0 mg. per kg. in 29 dogs. This dose was uniformly lethal within eighteen to twenty-four hours. In 10 dogs a smaller dose of endotoxin—0·05 mg. per kg.—was used. This produced prostration but did not cause death in any of the animals. This dose is hereafter referred to as a " sublethal " dose.

EXPERIMENTAL PROCEDURE

Sublethal Doses of Endotoxin in Intact Dogs

Blood samples were obtained before and two hours after the intravenous injection of 0·05 mg. per kg. of endotoxin in each of 10 dogs.

Lethal Doses of Endotoxin in Dogs with Adrenal-vein Cannulas

Specimens of peripheral and adrenal venous blood were obtained before, thirty minutes after, and two hours after the intravenous injection of 1·0 mg. per kg. of endotoxin. S.G.O.T. determinations were made on peripheral blood, and cortisol analyses on the timed adrenal venous blood samples. Minute outputs of cortisol were calculated. 11 animals were used.

S.G.O.T. LEVELS IN DOGS AFTER SUBLETHAL DOSES OF *Esch coli.* ENDOTOXIN

Dog no.	Control (units per ml.)	2 hours after intravenous *Esch. coli* endotoxin 0·05 mg. per kg. body-weight (units per ml.)
1	27	73
2	19	99
3	29	76
4	18	131
5	24	57
6	24	58
7	22	125
8	15	64
9	10	78
10	32	59
Mean	22	82

Lethal Dose of Endotoxin in Intact Dogs

Blood samples for S.G.O.T. and cortisol determinations were obtained before and thirty minutes, two hours, four hours, and six hours after the intravenous administration of 1·0 mg. per kg. of endotoxin in each of 12 dogs.

Lethal Dose of Endotoxin in Intact Dogs Given Intravenous Cortisol

6 animals were used. An intravenous injection of 100 mg. of cortisol dissolved in 2 ml. of distilled water (hydrocortisone sodium succinate, Upjohn), was given after blood samples were obtained. An infusion of 200 mg. of cortisol-free alcohol dissolved in 500 ml. of 5% dextrose solution in distilled water was begun and regulated to deliver 0·3 mg. of cortisol per minute throughout the experiment. Endotoxin (1·0 mg. per kg.) was injected intravenously and blood specimens were obtained for cortisol and S.G.O.T. determinations at 30 minutes and two, four, and six hours.

Results

Sublethal Doses of Endotoxin in Intact Dogs

These results are summarised in the accompanying table. All test animals had a febrile response within an hour of administration of endotoxin.

The control S.G.O.T. value rose from a mean of 22 units per ml. of serum (range 10–32 units per ml.) to a mean of 82 units per ml. of serum (range 57–131 units per ml.). This rise suggests that sublethal doses of endotoxin produce significant cellular injury.

Lethal Doses of Endotoxin in Dogs with Adrenal-vein Cannulas

The results of this experiment appear graphically in fig. 3. The S.G.O.T. values rose from a pre-endotoxin

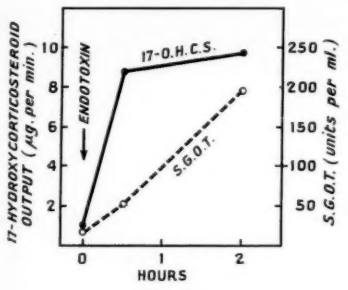


Fig. 3.

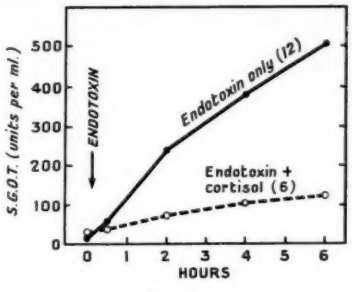


Fig. 4.

Fig. 3—The effect of a lethal intravenous injection of *Esch. coli* endotoxin on the output of cortisol from the right lumboadrenal vein and on peripheral-vein S.G.O.T. levels in dogs.

Fig. 4—S.G.O.T. activity after intravenous injection of a lethal dose of *Esch. coli* endotoxin with cortisol 0.3 mg. per min. and without cortisol.

control level of 16·6 units per ml. (range 10–28 units per ml.) to a mean of 192·4 units per ml. (range 108–357 units per ml.) in two hours. This rise is significantly greater than the rise recorded for dogs which received sublethal doses of endotoxin. The S.G.O.T. activity at thirty minutes was clearly increased with a mean value of 50·8 units per ml. (range 18–99 units per ml.).

The minute output of cortisol from the adrenal vein rose from a mean of 1·001 μg. per min. (range 0·369–2·50 μg. per min.) to a maximum of 9·64 μg. per min. (range 6·0–17·44 μg. per min.). This rise is slightly less than the rise observed after a single injection of 25 units of corticotrophin. Thus, adrenal secretory activity is near maximal after endotoxin.

Lethal Doses of Endotoxin in Intact Dogs

These results are shown in fig. 4. The sample usually collected at the end of thirty minutes was omitted in the first 5 animals. Plasma-cortisol levels were determined in 5 animals of this group. The mean control value for S.G.O.T. activity was 22·1 units per ml. of serum (range 10–35 units per ml.). The highest level of S.G.O.T. was found at the sixth hour with a mean of 504·1 units per ml. of serum (range 186–1080 units per ml.). The mean value at two hours was 236·3 units per ml. of serum in this group, whereas in the dogs given sublethal doses of endotoxin the mean value was only 82 units per ml. of serum. Apparently dose of endotoxin is directly related to degree of cellular injury. The plasma-cortisol values rose from a mean control of 14·4 μg. per 100 ml. of serum to a mean of 56·7 μg. per 100 ml. of serum at six hours. There was little variation of cortisol level throughout the experiment. The post-endotoxin cortisol levels are similar to those obtained after stimulation with corticotrophin. This accords with the observed increased adrenal secretory activity in the dogs with adrenal-vein cannulas.

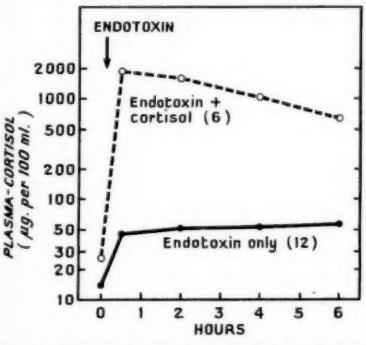


Fig. 5—Plasma levels of cortisol after a lethal intravenous injection of *Esch. coli* endotoxin with cortisol 0.3 mg. per min. and without cortisol.

Lethal Doses of Endotoxin in Intact Dogs Given Intravenous Cortisol

The results of this experiment are seen in fig. 5. Of the dogs in this group 3 survived lethal doses of endotoxin. Although the number of animals is not large enough to justify definitive conclusions, the increased survival suggests that cortisol protects to a variable degree against the lethal effect of endotoxin. Of more importance, however, is the insignificant rise in S.G.O.T. activity after endotoxin compared with that in the animals which did not receive cortisol.

The highest mean value at six hours is less than a quarter the value in dogs that did not receive cortisol. In the dogs that did not receive cortisol the six-hour mean S.G.O.T. level is twenty-five times the pre-endotoxin level, while in the cortisol-treated group the six-hour value is less than five times the pre-endotoxin level.

In the 3 dogs in which plasma-cortisol levels were determined, these were reciprocally related to the S.G.O.T. activity. The cortisol levels are plotted in fig. 5.

Discussion

If it can be assumed that S.G.O.T. activity mirrors cellular injury, these experiments suggest that: (1) endotoxin of *Esch. coli* produces cellular injury; (2) the degree of cellular injury is proportional to the dose of endotoxin administered; (3) cellular injury increases with time; and (4) cortisol significantly reduces the extent of cellular injury due to endotoxin when administered in doses exceeding physiological or pharmacological amounts. In dogs with endotoxin shock there is a continuous accelerated production of endogenous cortisol. But the blood and tissue levels of cortisol are inadequate for protection against the cellular injury induced by endotoxin. The levels of cortisol in the plasma appear to be the critical factor in the supply of hormone to the tissues. At physiological levels most of the steroid is bound to protein. Protein-binding, in a sense, confines the active steroid to the intravascular space. It is expedient, if large amounts of steroid are to be delivered to the tissues, to give a dose that greatly exceeds the protein-binding capacity of the plasma.

Dialysis experiments in our laboratory have demonstrated a direct relationship between the level of cortisol in the plasma and diffusible cortisol. These observations accord with the experience of Daughaday (1958). He has been unable to demonstrate a cortisol-binding globulin in canine peripheral blood, but has shown that the binding protein for cortisol in dog blood is albumin. In human blood the binding sites for cortisol on albumin are much more numerous than on globulin; the steroid-protein association is much weaker in the case of albumin, but this may not be true of canine blood.

The possibility that cortisol directly affects S.G.O.T. activity has been examined. In this laboratory when concentrations of cortisol up to 200 mg. per 100 ml. are added to plasma, S.G.O.T. activity is not influenced.

Summary

In dogs the intravenous injection of the endotoxin of *Esch. coli* produced a significant rise in serum-glutamic-oxalacetic-transaminase activity within two hours. The magnitude of the increment in transaminase activity was related to the administered dose of endotoxin.

The transaminase activity is probably an index of the cellular injury produced directly or indirectly by the endotoxin.

Adrenal secretory activity is near maximal after administration of endotoxin.

The simultaneous infusion of large quantities of cortisol (hydrocortisone) significantly interfered with the rise in transaminase activity after an injection of endotoxin. Similarly, the lethal effect of endotoxin was reduced.

These findings provide further evidence that cortisol suppresses the toxic effects of endotoxins produced by gram-negative bacteria.

REFERENCES

Abernathy, R. S., Spink, W. W. (1958) *J. clin. Invest.* **37,** 219.
Daughaday, W. H. (1958) *Arch. intern. Med.* **101,** 286.
Farrell, G. L. (1954) *Proc. Soc. exp. Biol., N.Y.* **86,** 338.
Halberg, F., Spink, W. W., Bittner, J. J. (1956) *Endocrinology,* **59,** 380.
Hall, W. H., Gold, D. (1955) *Arch. intern. Med.* **96,** 403.
Hume, D. M., Nelson, D. H. (1955) *Surg. Forum Amer. Coll. Surg.* **5,** 568.
Jacob, S., Weizel, H., Gordon, E., Korman, H., Schweinburg, F., Frank, H., Fine, J. (1954) *Amer. J. Physiol.* **179,** 523.
Karmen, A., Wroblewski, F., LaDue, J. S. (1955) *J. clin. Invest.* **34,** 126.
Mansberger, A. R., Ochsner, E. W. A., Jacob, S., Oppenheimer, J. H., Gillette, R. W. (1958) *Surgery,* **43,** 708.
Melby, J. C., Egdahl, R. H., Spink, W. W. (1957) *Fed. Proc.* **16,** 425.
— Spink, W. W. (1958) *J. clin. Invest.* **37,** 1.
Peterson, R. W., Karrer, A., Guerra, S. L. (1957) *Analyt. Chem.* **29,** 144.
Silber, R. H., Porter, C. C. (1954) *J. biol. Chem.* **210,** 923.
Spink, W. W. (1957) *New Engl. J. Med.* **257,** 979.
— Anderson, D. (1954) *J. clin. Invest.* **33,** 540.
— Hall, W. H. (1952) *ibid.* **31,** 958.
Sugiyama, H., Bergdoll, M. S., Dack, G. M. (1958) *Proc. Soc. exp. Biol., N.Y.* **98,** 33.
Thomas, L. (1958) *A.M.A. Arch. intern. Med.* **101,** 452.
Waisbren, B. A. (1951) *ibid.* **88,** 467.
Watson, D. W. (1957) *Fed. Proc.* **16,** 437.
Weil, M. H., MacLean, L. D., Visscher, M. B., Spink, W. W. (1956) *J. clin. Invest.* **35,** 1191.
— Spink, W. W. (1958) *A.M.A. Arch. intern. Med.* **101,** 184.
Wroblewski, F. (1956) *Trans. N.Y. Acad. Sci.* **18,** 444.

ATHEROSCLEROSIS AND ISCHÆMIC HEART-DISEASE

OBSERVATIONS IN JAMAICA

W. B. ROBERTSON
M.B., B.Sc. St. And.

SENIOR LECTURER IN MORBID ANATOMY,
UNIVERSITY COLLEGE OF THE WEST INDIES, JAMAICA

MANY workers have concluded that populations living on high-calorie high-fat diets have a higher mean serum-cholesterol, and are more prone to ischæmic heart-disease, than those living on simpler diets. But much of the evidence for this thesis is circumstantial, and it is the less easily assessed because until recently no method had been used by which the actual morbid-anatomical incidence of atherosclerosis in different groups or races could be compared. Reliance has been placed upon impressions or inferences from clinical data. This has prompted two groups of workers (Gore and Tejada 1957, Holman et al. 1958a) to devise techniques which would allow valid comparison, and the results of comparative studies so far published (Tejada and Gore 1957, Holman et al. 1958b, Strong et al. 1958, Tejada et al. 1958) indicate that this method of study will do much to substitute facts for assumptions.

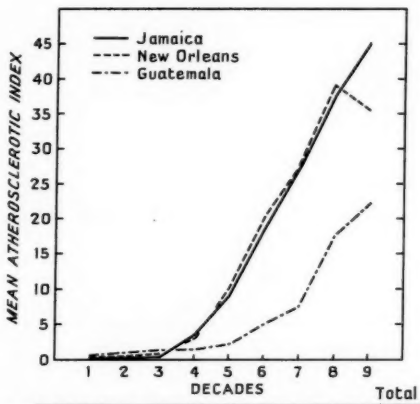
For my survey of aortic atherosclerosis in Jamaica I used the method of Gore and Tejada.

At necropsy the aorta, after being opened by a posterior longitudinal incision, is retained intact, from the aortic-valve ring to the bifurcation, and is fixed in the usual manner in 10% neutral buffered formal-saline. At the time of necropsy or after fixation, it is "read": the total surface area involved by disease is assessed, and an estimate is made of the percentage involvement by each of four grades—namely, fatty streaks; fibrous (pearly) plaques; necrotic, ulcerated, or hæmorrhagic plaques; and calcified plaques. A "profile" of the disease is thus obtained, and by the application of a simple formula an "atherosclerotic index" can be calculated. This will vary from 0 to 100, according to the types of lesion and area involved.

500 aortas have been studied, from consecutive necropsies at the University College Hospital of the West Indies—a general hospital of some 300 beds. The population served by this hospital is partly urban and partly rural, and the patients are nearly all from the poorer section of the community. Most of them are Negros, but a few are pure East Indian, Chinese, or Caucasian, and some of mixed racial origins.

Findings

For purposes of comparison my findings have been coordinated with those of Tejada and Gore (1957), who compared aortic atherosclerosis in Guatemala and New Orleans. The chart shows that there is no appreciable



NO. OF CASES										Total
J.	154	31	29	37	76	71	62	31	9	500
NO.	158	68	74	73	52	65	69	30	27	616
G.	31	20	39	62	50	47	44	22	9	324

difference between the three groups until after the third decade, when they diverge. The Jamaican and New Orleans groups show an almost identical upward trend, but this is not seen in the Guatemalan group until the fifth and sixth decades, and even then is less steep. In their middle and later decades, the Jamaican and New Orleans groups have an ever-increasing incidence of the more advanced lesions of atherosclerosis, and the average area involved also increases, though to a lesser extent. The pattern in Jamaica is for all practical purposes the same as the pattern in New Orleans.

Tejada and Gore found that in their two groups the incidence of atherosclerosis ran parallel to the incidence of ischæmic heart-disease, which is common in New Orleans but very rare in Guatemala. But this parallelism does not apply to Jamaica, where the incidence of atherosclerosis is high but the incidence of ischæmic heart-disease is rela-

tively low—being far below that of New Orleans and not very much higher than that of Guatemala (table I). Furthermore, two of the Jamaicans with ischæmic heart-disease were of pure East Indian extraction, and one was a Caucasian—races which constitute only a very small fraction of the total group studied. We must conclude that the Jamaican Negro, while developing a degree of aortic atherosclerosis comparable to that obtaining in the United States of America, only occasionally succumbs to ischæmic heart-disease.

TABLE I—MYOCARDIAL INFARCTION IN PERSONS AGED 40 YEARS AND OVER

—	Total no. of cases	No. of infarction cases	Percentage
New Orleans ..	316	51	16·1
Guatemala ..	234	1	0·4
Jamaica ..	249	6	2·4

TABLE II—JAMAICAN CASES OF MYOCARDIAL INFARCTION

Age	Sex	Race	Atherosclerotic index	Mean index for decade
65	M	Negro	55·0	27·3
69	F	Negro	4·4	27·3
47	M	East Indian	26·2	9·1
60	M	East Indian	46·0	27·3
73	M	Negro	37·0	38·3
59	M	Caucasian	25·3	18·9

It should be noted, however, that the atherosclerotic indices of the Jamaican cases of myocardial infarction are in general higher than the means of the age-groups in which they occur (table II). Possibly a certain degree of atherosclerosis is required before coronary occlusion can take place.

Discussion

The first question is whether this method of assaying atherosclerosis is accurate enough to allow comparison of series from different centres. After experience with over a thousand cases Gore and Tejada were satisfied that the method "is practical, and yields reasonably consistent results".

Probably the greatest difficulty arises in distinguishing between simple fatty streaks and fibrous plaques, for the point at which one merges into the other is very much a matter of interpretation. In this method, however, the important differentiator is the incidence of what are termed the complicated lesions, such as ulceration, necrosis, hæmorrhage, and calcification in plaques; and no difficulty is encountered in their assessment. In constructing their formula for the atherosclerotic index Gore and Tejada gave these features special weighting factors, in view of their probable importance in initiating the clinical manifestations of disease; and thus, intentionally or otherwise, they gave prominence to those features of atherosclerosis which are most easily and accurately assayed. Even if the method is considered relatively crude, it has the great merit of forcing the observer to make an objective assessment of the disease, as accurately as he can by purely visual means. The terms mild, moderate, severe, gross, and others traditionally employed are worthless for purposes of comparison. Because our knowledge of the incidence of atherosclerosis—not of ischæmic heart-disease—throughout the world is at present very incomplete, some standardised method is urgently required (World Health Organisation Report 1958).

The second question is whether there is any relation between the degrees of aortic and coronary atherosclerosis. At first sight it would seem unlikely that a disease which is thought to be associated in some way with lipid metabolism should pick out different parts of the vascular system in an apparently haphazard way from case to case and even within the same patient; yet such is the experience of most observers (Winter et al. 1958). What has impressed me in Jamaica is that, although aortic atherosclerosis is seen in its severest forms, and atheromatous plaques are common enough in the coronary arteries of the older people, stenosing lesions and occlusions in the coronaries are rarely to be found. Similar observations have been made in the South African Bantu by Higginson and Pepler (1954), Laurie and Woods (1958), Becker (1958), and Walker and Simpson (1958). This lack of correlation between aortic atherosclerosis and coronary occlusion has often been commented on (Duguid and Robertson 1955).

Racial Factors

That differences in disease patterns are due to purely ethnic factors is difficult to prove or disprove, because it is often well-nigh impossible to neutralise a host of other factors.

Holman et al. (1958b) have demonstrated that the difference between the Whites and Negros in New Orleans up to the age of 40 is that the Negro has significantly more deposition of lipid in the aorta about the time of puberty but has a lesser, or delayed, tendency to convert the fatty streaks to fibrous plaques. They offered no explanation for this apparent anomaly and tended to discount such factors as diet and mode of life.

Unfortunately Tejada and Gore (1957) did not think their numbers justified separate assessments of the White and Negro in their New Orleans material. If Holman's assertion concerning the differences between the two races in New Orleans holds true after the age of 40, the figures from the Negro section of their New Orleans assay might have depressed the mean indices for the later decades. They could not, however, have reduced them to parity with the Jamaican figures. Nor is there any indication from their total of myocardial infarctions as to how many occurred in Negros and how many in Whites.

From the data accumulated in Jamaica and New Orleans it would seem that Negros are as liable as Whites to develop severe aortic atherosclerosis but preserve a fortunate freedom from ischæmic heart-disease.

Dietary Factors

Judged by British or American standards, the diet of the poorer Jamaicans is high in carbohydrate and low in first-class protein (Tulloch 1958). Coconut oil is used extensively in cooking and some animal fat is eaten. While this type of diet may prove to be atherogenic, by virtue of the quantity or quality of fat it contains, it evidently does not predispose to occlusive coronary-artery disease. From this we may conclude that atherogenic properties in a diet cannot be held responsible for ischæmic heart-disease.

The Thrombogenic Factor

Duguid (1954) has shown that the classical picture of atherosclerosis is produced in the coronary arteries by the organisation and subsequent degeneration of occluding and mural thrombi.

Morris (1951), when he could find no evidence of an increase in atherosclerosis in necropsies at the London Hospital over a period of forty years, urged that closer attention be paid to the mechanism of occlusion of the coronary arteries. Workers in South Africa have been impressed with the relative rarity of stenosing and occlusive coronary-artery disease in Negros with severe

aortic atherosclerosis, and my experience in Jamaica has been the same: not only is coronary thrombosis relatively uncommon, but so are cerebral thrombosis (though not cerebral hæmorrhage), phlebothrombosis, and pulmonary embolism. It is noteworthy that, parallel with the decrease in ischæmic heart-disease in Scandinavia during the second world war, there was a drop in the number of thrombo-embolic phenomena observed in surgical clinics (Closs and Dedichen 1949). Schornagel (1955) showed that the rise in myocardial infarction observed in Holland after the war was due to an increase in actual thromboses in the coronary arteries rather than to any increase in atherosclerosis.

We appear, then, to be confronted by two separate, though possibly related, diseases—chronic atheromatous degeneration and acute coronary thrombosis. The fact that the latter is seldom seen in the absence of the former need not imply a common ætiology; and one is bound to ask why, of two individuals (or populations) with atherosclerosis, one dies of coronary thrombosis but the other does not.

Summary and Conclusions

Using a standardised technique, the incidence of atherosclerosis of the aorta at 500 necropsies in Jamaica has been compared with the incidence in published series in which the same method was employed.

The predominantly Negro population in Jamaica develops a degree of aortic atherosclerosis similar to that of a mixed population in New Orleans, U.S.A.

The incidence of myocardial infarction, however, is much lower in the Jamaican series.

Other thrombotic diseases are also rarer in Jamaica.

Since there is no constant relation between the incidence of atherosclerosis and the incidence of coronary thrombosis, they are very unlikely to have the same cause. Atherosclerosis may or may not be promoted by a dietetic factor; but, if it is, the same factor can hardly be responsible for the thrombosis which results in ischæmic heart-disease.

In ætiological studies the two conditions need to be clearly distinguished. Since advanced atherosclerosis is compatible with health and long life, investigation of the cause of thrombosis is of more immediate concern.

My thanks are due to Dr. Ira Gore, of Boston, Mass., for introducing me to the method of assaying atherosclerosis, and for his kindness in checking the readings of a number of specimens sent to him; to Dr. Carlos Tejeda, of Guatemala, who performed a similar check; and to Prof. G. Bras for his encouragement and advice.

REFERENCES

Becker, B. J. P. (1958) *Lancet*, i, 1019.
Closs, K., Dedichen, J. (1949) *ibid.* ii, 1242.
Duguid, J. B. (1954) *ibid.* i, 891.
— Robertson, W. B. (1955) *ibid.*, 525.
Gore, I., Tejeda, C. (1957) *Amer. J. Path.* **33**, 875.
Higginson, J., Pepler, W. J. (1954) *J. clin. Invest.* **33**, 1366.
Holman, R. L., McGill, H. C., Jr., Strong, J. P., Geer, J. C. (1958a) *Lab. Invest.* **7**, 42.
— — — — (1958b) *Amer. J. Path.* **34**, 209.
Laurie, I. M., Woods, J. D. (1958) *Lancet*, i, 231.
Morris, J. N. (1951) *ibid.* i, 1, 69.
Schornagel, H. E. (1953) *Docum. Med. geogr. trop.* **5**, 173.
Strong, J. P., McGill, H. C., Jr., Tejada, C., Holman, R. L. (1958) *Amer. J. Path.* **34**, 731.
Tejada, C., Gore, I. (1957) *ibid.* **33**, 887.
— — Strong, J. P., McGill, H. C., Jr. (1958) *Circulation*, **18**, 92.
Tulloch, J. A. (1958) *Med. Pr.* **240**, 866.
Walker, A. R. P., Simson, I. W. (1958) *Lancet*, i, 1126.
Winter, M. D., Sayre, G. P., Millikan, C. H., Barker, N. W. (1958) *Circulation*, **18**, 7.
World Health Organisation (1958) Technical Report Series, no. 143.

DORSAL KYPHOSIS IN CHRONIC OBSTRUCTIVE LUNG DISEASE

DENIS F. J. HALMAGYI *
M.D. Szeged

From the Miners' Chest Diseases Treatment Centre and the Pneumoconiosis Research Unit (Medical Research Council), Llandough Hospital, near Cardiff

TEXTBOOKS used to include kyphosis among the common signs of chronic obstructive chest disease; but since a mild backward curve in the thoracic spine is physiological (Epstein 1955) the deformity is difficult to assess (Fletcher 1952). Hippocrates noticed the relation between dorsal kyphosis and dyspnœa, but only in 1939 did Chapman et al. report a large-scale investigation. They found that kyphosis significantly diminished cardiorespiratory efficiency and could lead to failure (Kerwin 1942), but they did not investigate its effect on an already damaged cardiopulmonary system.

In the present investigation I have adopted a simple and objective way of measuring the spinal curve in patients with and without lung disease; and I have correlated it with other signs of chronic obstructive chest disease.

Material and Methods

Groups of Patients

I investigated two groups of patients.

Group I consisted of 300 patients admitted to the Miners' Chest Diseases Treatment Centre for respiratory complaints: they were all miners or ex-miners who had retired because of age or respiratory disability. The diagnoses were pneumoconiosis (simple or complicated), primary obstructive emphysema, or bronchial carcinoma. Some had pulmonary heart-disease but none suffered from any extrapulmonary illness.

Group II consisted of 60 patients. 50 were selected from the past ten years' records of the Llandough Hospital: they were coalminers whose age and occupational history were similar to those of patients in group I, but none of whom had respiratory complaints. Their chest X-ray films were normal. The diagnoses included gastric and duodenal ulcer, hypertension, coronary-artery disease, gallstones, and neurosis. The

* Present address: Department of Medicine, University Medical School, Sydney, Australia.

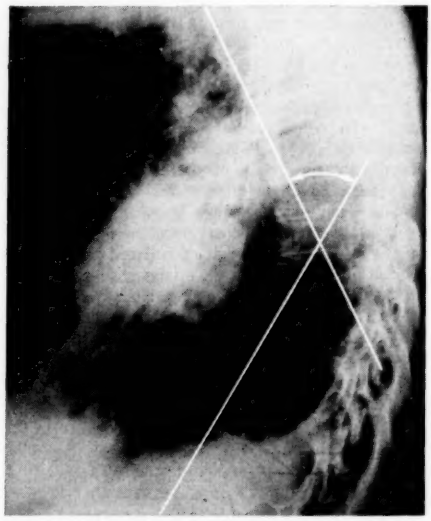


Fig. 1—Method of measuring the kyphotic angle.

remaining 10, though first admitted to the treatment centre, proved to be free from lung disease and were mostly neurotics.

Measurement of Ventilatory Capacity

The indirect maximal breathing capacity (M.B.C.) was determined in all patients in group I and in the last 10 patients in group II.

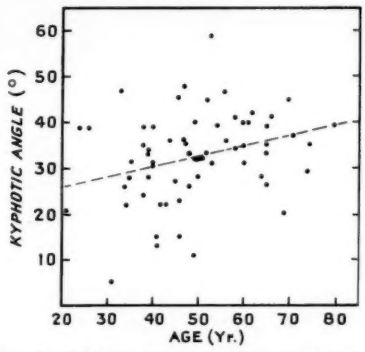


Fig. 2—Relation between kyphotic angle and age in coalminers without respiratory disease.

The apparatus and procedure has been described by Gaensler (1951) and Kennedy (1953). A mean of three separate determinations was calculated: the difference between single measurements never exceeded 10%.

Measurement of Kyphosis

Lateral chest X-ray films were used if they gave a clear picture of the entire spine.

Tangents were drawn to the anterior borders of the second and eleventh thoracic intervertebral spaces (fig. 1). The angle facing upwards—called the "kyphotic angle"—was measured with a protractor in 28 patients, twice on two separate films of each patient. The mean kyphotic angle was 46°. In 3 the two measurements differed by 4°; in 5 by 3°; and in the rest by 0–2°. Three measurements on three separate films were made in 13 patients. Their mean kyphotic angle was 49°: in 1 the results differed by 6°; in 2 by 5° and 4° respectively, and in the rest by 0–3°.

Other X-ray Changes

Exostoses, calcification of the anterior ligament, and irregularity of the intervertebral space, with or without calcium deposits, suggested non-specific osteoarthritis (Schmorl and Junghans 1951, Kellgren and Lawrence 1952, Epstein 1955). Special significance was attached to wedging or collapse of a single vertebra.

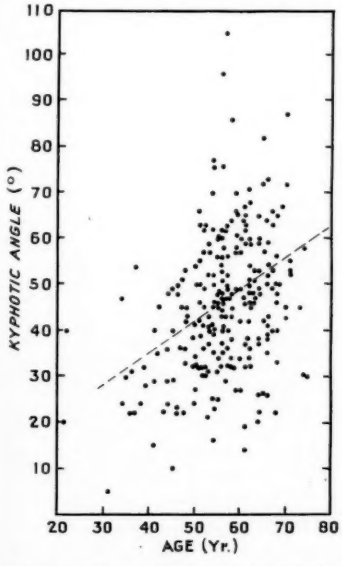


Fig. 3—Relation between kyphotic angle and age in coalminers with chronic obstructive lung disease.

Electrocardiography

Pulmonary hypertension was diagnosed or excluded on routine electrocardiograms (Halmagyi 1957).

No patient in group I had coronary-artery disease, valvular defect, or a brachial arterial diastolic pressure above 100 mm. Hg. Tracings of standard, QVR, QVL, QVF, and V_1, V_4, V_6 leads were interpreted by Dr. A. J. Thomas as outlined by him previously (Gilson and Hugh-Jones 1955).

Results

The relation between age and curvature of the spine in the controls (group II) is shown in fig. 2.

The regression equation was:

$$Y = 21{\cdot}5 + 0{\cdot}220\ X$$

where X was the age in years and Y the kyphotic angle in degrees. The correlation coefficient was 0·278 and the regression coefficient 0·220 (± 0·106) $P < 0{\cdot}05$.

The relation of age to curvature of the spine in patients with chronic obstructive lung disease (group I) is shown in fig. 3. It differs from that found in the control group ($0{\cdot}05 > P > 0{\cdot}02$) both in the overall degree of kyphosis and in its annual increase.

In group I between the ages of 35 and 44 the angle increases by 0·14° every year, between 45–54 by 1·88°, and between 55 and 64 by 0·55°. Between 65 and 74 the angle decreases by 0·46° every year. Though these slopes do not differ significantly, there is evidence ($P \ll 0{\cdot}01$) that the overall relationship is curved. The maximum change is somewhere between 55 and 70 years. Nevertheless, in correcting kyphosis for age adequate allowance can be made by assuming a linear relationship over all age-groups, the angle increasing by 0·68° every year.

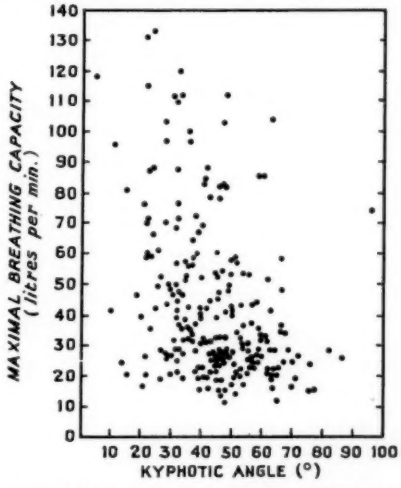


Fig. 4—Relation between indirect M.B.C. and kyphotic angle in coalminers with chronic obstructive lung disease.

The relation between kyphotic angle and M.B.C. in chronic obstructive lung disease is shown in fig. 4.

With M.B.C. expressed in litres per minute, the regression equation was

$$Y = 24{\cdot}5 - 0{\cdot}138 \times \text{MBC} + 0{\cdot}462\ X$$

This means that when the kyphotic angle increases by 0·138°, the maximum breathing capacity diminishes by 1 litre per minute.

Pathological changes of the thoracic spine were more prevalent in group I than in group II (fig. 5). In an attempt to establish a relation between the kyphotic angle and electrocardiographic signs of pulmonary hypertension, patients in group I were divided into three subgroups (fig. 6). The first subgroup consisted of 18 patients with left axis deviation, the second of 100 patients without axis deviation, and the third of 86 patients with right axis deviation. The mean age of the subgroups was similar, and there was very little difference between their mean kyphotic angles; but the mean M.B.C. values were strikingly different. They were highest in the subgroup

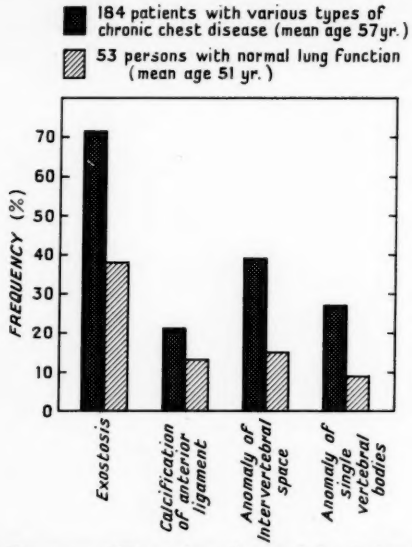


Fig. 5—Frequency of X-ray signs characteristic of chronic non-specific spinal osteoarthritis in coalminers with and without respiratory disease.

with left ventricular hypertrophy and lowest in the subgroup with right axis deviation.

Discussion

Around the age of 30 the mean angle of the dorsal spine is nearly similar in miners with and without chronic obstructive chest disease. With advancing age, however, miners with lung disease become more kyphotic than miners with healthy chests. The significant negative correlation between the curvature of the thoracic spine and the maximum breathing capacity points to the diminished ventilatory capacity of patients with kyphosis.

Spinal osteoarthritis becomes more common with age, and it affects miners more often than people doing less strenuous work (Gautenberg 1929, 1930, Baader 1951, Kellgren and Lawrence 1952). The only difference between the two groups of miners in the present investigation was the absence of respiratory disease in group II. In a post-mortem study of the spines of emphysematous subjects, Kountz and Alexander (1933) found that the commonest lesion was disease of the intervertebral discs, leading to erosion of the vertebral bodies and consequent kyphosis. My conclusion is similar to theirs: an increased tendency to dorsal kyphosis is probably related to the earlier onset and greater prevalance of chronic osteoarthritis.

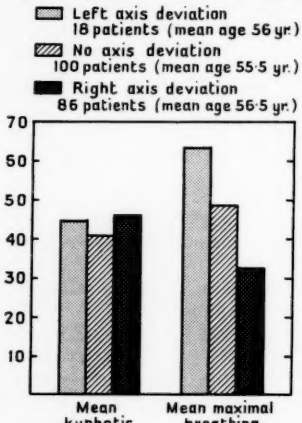


Fig. 6—Correlation of kyphotic angle and M.B.C. with electrocardiographic signs of pulmonary hypertension in coalminers with chronic respiratory disease.

There is no evidence that chronic lung disease can result in spinal osteoarthritis. On the other hand, ankylosing spondyloarthritis is often associated with a reduced total and vital lung capacity (Hart et al. 1949, D'Silva et al. 1953, Rogan et al. 1955) and a tendency to bronchial infections and atelectasis (Hamilton 1949). It seems as though loss of spinal mobility, with or without kyphosis, might affect adversely both lung function and resistance to infection. This would explain why spinal anomalies are so often found in respiratory cripples.

Chest pain is very common in chronic obstructive lung disease: in some cases it is due to coronary-artery disease or pulmonary hypertension; but in others it resembles the pain of spinal osteoarthritis.

Kyphosis in chronic respiratory disease should be remembered when correlating M.B.C. or other lung-function tests with height or stem-height. A change in height may be secondary to the pulmonary condition.

Lack of correlation between electrocardiographic changes of right ventricular hypertrophy and the degree of kyphosis does not strengthen the traditional concept of "kyphoscoliotic heart disease". For more than a century pulmonary hypertension in kyphosis was attributed to kinking of the great vessels, but more recent studies have shown that pulmonary hypertension is related not to the kyphosis but to the parenchymal lung damage (Schaub et al. 1954, Gray 1956). In my series right ventricular hypertrophy was common in patients whose extensive lung damage was shown by their low M.B.C.; but it was not unduly prevalent in patients with kyphosis.

Summary

Osteoarthritis of the spine was investigated in 300 patients with chronic obstructive lung disease and in 60 patients of comparable age with no respiratory complaints. Both groups consisted of coalminers.

Around the age of 30 the angle of kyphosis was about equal in the two groups, but with advancing age miners with diseased chests became more kyphotic. Non-specific chronic osteoarthritis of the spine was also more common in this group.

The indirect maximum breathing capacity showed a significant negative correlation to the kyphotic angle. Electrocardiographic signs of right ventricular hypertrophy were related to the maximum breathing capacity but not to the degree of kyphosis.

The statistical methods used in this investigation were suggested by Mr. P. D. Oldham. Calculations were carried out by Miss Barbara Snow. Their invaluable help is gratefully acknowledged.

REFERENCES

Baader, L. (1951) *Rheumaforsch.* **10,** 135.
Chapman, E. M., Dill, D. B., Graybiel, A. (1939) *Medicine,* **18,** 167.
D'Silva, J. L., Freeland, D. E., Kazantzis, G. (1953) *Thorax,* **8,** 303.
Epstein, B. S. (1955) The Spine. London.
Fletcher, C. M. (1952) *Proc. R. Soc. Med.* **45,** 577.
Gaensler, E. A. (1951) *Science,* **114,** 444.
Gautenberg, R. (1929) *Fortschr. Röntgenstr.* **39,** 650.
— (1930) *ibid.* **42,** 740.
Gilson, J. C., Hugh-Jones, P. (1955) Lung Function in Coalworkers' Pneumoconiosis. Medical Research Council Special Report. London.
Gray, F. D., Jun. (1956) *J. chron. Dis.* **4,** 499.
Halmagyi, D. F. J. (1957) Die klinische Physiologie des kleinen Kreislaufs. Jena.
Hamilton, K. A. (1949) *Ann. intern. Med.* **31,** 216.
Hart, F. D., Robinson, K. C., Allchin, F. N., Maclagan, N. F. (1949) *Quart. J. Med.* **18,** 217.
Kellgren, J. H., Lawrence, J. S. (1952) *Brit. J. industr. Med.* **9,** 197.
Kennedy, M. C. S. (1953) *Thorax,* **8,** 73.
Kerwin, A. J. (1942) *Arch. intern. Med.* **69,** 560.
Kountz, W. B., Alexander, H. L. (1933) *J. Amer. med. Ass.* **100,** 551.
Rogan, M. C., Needham, C. D., McDonald, I. (1955) *Clin. Sci.* **14,** 91.
Schaub, F., Bühlmann, A., Kachlin, R. (1954) *Cardiologia,* **25,** 147.
Schmorl, G., Junghans, H. (1951) Die gesunde und kranke Wirbelsäule im Röntgenbild und Klinik. Stuttgart.

PULMONOCARDIAC FAILURE
ASSOCIATED WITH DEFORMITY OF THE CHEST

MERVYN L. ABRAHAMSON
M.D. Dubl., F.R.C.P.I.
ASSISTANT PHYSICIAN AND PHYSICIAN IN CHARGE OF THE CARDIAC DEPARTMENT, RICHMOND (ST. LAURENCE'S) HOSPITAL, DUBLIN

A FEW years ago a fatal case of pulmonocardiac failure in a patient with kyphoscoliosis aroused my interest in the relationship of deformities of the chest to disease of the lungs and heart. There was little in the literature about this subject, though attention had been drawn to the difficulty of interpreting physical signs in the presence of asymmetry, and to the psychological trauma in those sensitive about their deformity. In 1939, however, Chapman et al. had reviewed 126 fatal cases, in 79 of whom the average age at death was 30 years; in particular severe kyphoscoliosis and pectus excavatum were likely to be associated with pulmonary and cardiac failure.

Pectus excavatum is generally attributed to a congenital defect of the diaphragm, possibly a short central tendon (Brown 1939). It is this concept that has allowed successful surgery to be carried out (Chin and Adler 1954). The cause of kyphoscoliosis is more obscure. Chapman et al. (1939) suggested unrecognised poliomyelitis as the chief cause, and mentioned also congenital or hereditary defects, rickets, and tuberculosis. They did not refer to trauma, which appears to have been the factor in both my fatal cases. They described increasing dyspnœa as the main symptom, with a tendency to paroxysmal attacks and sometimes with bouts of weakness and fainting. They mentioned also palpitation, cough, and epistaxis, but stated that precordial pain was rare, and that hypertension was probably not a feature, though a rise in diastolic blood-pressure had been recorded.

The cause of symptoms in these cases remains uncertain. In a recent paper on heart-failure of the hunchback, Hanley et al. (1958) suggest that in the presence of kyphoscoliosis heart-failure is a consequence of impaired lung function, though the mechanism is obscure. In my two fatal cases mechanical factors seem to offer at least a partial explanation.

THE FIRST CASE

A man, aged 39, with gross kyphoscoliosis of the dorsal spine dating from an injury in childhood, presented with dyspnœa, cyanosis, and periods of mental confusion, which were eased by lying face down over the side of the bed. He died shortly after admission to hospital. The main changes at necropsy were collapse of areas of both lungs, flattening of the trachea in a " sabre " fashion, enlargement of the right auricle and both ventricles, and marked atheroma of the aorta with partial occlusion of the coronary arteries. Section of the kidneys revealed changes of early hypertension (the blood-pressure had been essentially normal).

All his symptoms could be correlated with the pathological findings. The dyspnœa, cyanosis, and enlargement of the right side of the heart appeared to result from kinking of the pulmonary artery, compression of the trachea, and pulmonary collapse. The attacks of mental confusion and the left ventricular enlargement could be explained by kinking of the aorta. (My father and I first reported this case in 1949.)

THE SECOND CASE

A spinster, aged 47, complaining of chest pain, breathlessness, giddiness, and palpitation, was admitted to hospital on Dec. 7, 1956.

She had first noticed severe headaches about 6 years previously, when she was found to have hypertension. 4 years later she started to get attacks of anginal pain, which sometimes came on at rest, but were especially precipitated by exertion or emotional upset. Her breathing became laboured on any physical effort.

On examination she was anxious, obviously undersized (height 4 ft. 10 in.), and grossly deformed, with a mid-dorsal kyphosis which appeared to be the result of an injury at the age of 2 necessitating a year's stay in hospital. Over the deformed area of the spine there was increased vascularity and discoloration of the skin. The chest was grossly distorted, being very wide and short, with narrowing of the intercostal spaces. As a result the interpretation of physical signs was very uncertain, but pulsation could be felt in the 4th left interspace in the mid-clavicular line. There was tachycardia. In the pulmonary area a short, blowing systolic murmur and a double 2nd sound could be heard. The blood-pressure was 220/130 mm. Hg, with little difference in the two arms. The optic fundi showed moderate arteriosclerotic changes. There were no abnormal neurological signs, so that despite the gross kyphosis the spinal cord did not appear to have suffered.

An electrocardiogram (E.C.G.) showed multiple T-wave inversion, peaked P-waves in leads I and II, and poor P-waves in lead III. The chest leads were misleading as the deformity made accurate placing of the electrode difficult. Nevertheless, the findings were compatible with a diseased myocardium. A radiograph of the chest showed gross distortion of the thorax and its contents. The cardiac shadow was enormous and globular, touching the chest wall on each side. The aortic arch was diverted to the left. The lung fields were clear. A blood-count revealed a mild hypochromic anæmia (Hb 82%). The urine was normal.

About a fortnight after admission she had an acute attack of dyspnœa followed by a fall in blood-pressure (125/90). An E.C.G. taken at this time showed a prominent Q-wave in lead III, which was not previously seen; T_2 had become upright, but this might have been due to a misplaced electrode. A few days later (Dec. 26) she developed mild dysphasia; we felt this was due to the drop in blood-pressure, causing deterioration in the blood-flow to the brain.

Over the next few weeks her condition improved and she was then allowed up for short periods. On Feb. 17 she had a further attack of left ventricular failure, with pulmonary œdema and a drop in systolic blood-pressure to 50 mm. Hg. After treatment with intravenous aminophylline and nikethamide she improved. For the next few days she complained of vague discomfort across her chest; the heart sounds were much feebler, and the systolic blood-pressure was about 100. Accordingly, we thought she had had a myocardial infarction which was atypical in that dyspnœa overshadowed pain. This diagnosis was confirmed by E.C.G. For a few days she seemed to improve, but on Feb. 27 she died suddenly.

At necropsy the 7th dorsal vertebra (in the region of the kyphosis) could not be demonstrated. The ribs were extremely crowded. There was no evidence of gross lung damage. The aorta, which was atheromatous, was nipped in the angulation of the spine. There was gross left ventricular hypertrophy. The descending branch of the left coronary artery was the site of a thrombus. The liver was enlarged showing signs of chronic venous congestion, and the spleen also was congested. The kidneys were unaffected apart from very slight hypertensive changes. The vessels at the base of the brain were arteriosclerotic, and there was a small area of cerebral softening in the left temporal lobe. Death was attributed to occlusion of the left coronary artery.

THE THIRD CASE

A 17-year-old messenger boy was admitted to hospital on May 17, 1957, with deformity of the chest, tiredness, and occasional fainting attacks.

He had a moderate degree of pectus excavatum, and this was confirmed by radiography. The apex-beat, which was diffuse, appeared to be in the 5th left interspace in the anterior axillary line. The heart sounds were normal, and a soft systolic

murmur could be heard over the precordium. The blood-pressure was 110/70 mm. Hg. The E.C.G. showed some peaking of the P-waves in leads II and III, with inverted T-waves in lead III, and RSR-complexes in V_2. All other investigations were normal.

Operation was decided upon and carried out by Mr. C. K. Byrnes on July 27, the deformity being corrected by elevation of the sternum after resection of the 2nd to 7th costal cartilages, and sawing and partly breaking the manubriosternal joint. The sternum was kept in position by a pin which was left in situ for about 5 weeks.

His immediate postoperative course was troublesome because of carbon-dioxide retention and elevation of the blood-pressure. This was corrected by careful administration of oxygen to wash out the carbon dioxide. Ultimately he made an excellent recovery, and was discharged in November.

I feel that this case is of some practical importance, for the postoperative difficulty with carbon dioxide was certainly exaggerated by, if not due to, rigidity of the chest wall. This would presumably be less of a problem in cases operated on in early childhood.

THE FOURTH CASE

A male shop-assistant, aged 29, complaining of breathlessness on mild exertion and tiredness, was admitted to hospital on March 14, 1957. He had first noticed breathlessness in 1949. It had persisted since, varying in degree from time to time, and precipitated by exertion, but several times it had reached sufficient severity to necessitate his temporarily giving up work.

He had fallen down a flight of stairs at the age of 9 and injured his spine so badly that he was in hospital for 4 years.

On examination there was much crowding of the ribs, and the chest appeared unduly broad and squat. Respiratory movement was obviously diminished, and a few scattered rales could be heard over both lungs. The heart-rate averaged 90 per min., and the pulmonary 2nd sound was slightly accentuated. Radiography confirmed the crowding of the ribs; the heart appeared normal. An E.C.G. showed tachycardia with inversion of the T-wave in lead III. The vital capacity was 60% of normal. All other investigations were normal.

It was felt that the symptoms were purely respiratory in origin and that if he could be taught to use his respiratory muscles more efficiently improvement might follow. Accordingly, intensive breathing exercises were started. The response was so satisfactory that he was able to leave hospital, fully active and free from symptoms, in just over 2 months.

He was asked to continue his exercises, and to return for reassessment. He has not returned, and so I do not know whether the improvement has been maintained.

Discussion

With recent improvements in thoracic surgery, the relationship of chest deformity to disease of the heart and lungs has become more important. There is now general agreement that pectus excavatum is not a benign condition, though mild forms are compatible with a normal existence. Chin and Adler (1954) think that all cases should be operated on unless they are too young or too old. Wachtel et al. (1956) hold that surgery is indicated in children with much deformity or in whom deformity is progressing, and in adults with symptoms. The findings of Chapman et al. (1939), and of Hanley et al. (1958) show that kyphoscoliosis is an important cause of heart-disease. This view is confirmed by my two fatal cases.

The basis of cardiac disturbance in the deformed chest remains in dispute. Wachtel et al. (1956) enumerate the following factors: (1) decreased return of blood to the right side of the heart, (2) cardiac arrhythmias secondary to atrial impingement, (3) restriction of expansion of the heart, and (4) a decrease in respiratory reserve. In regard to the last, even in the mildest of my cases there was evident decrease in respiratory reserve.

In the hunchbacks described by Hanley et al. (1958), it seemed that heart-failure was most likely to supervene in those with severe impairment of lung function. Anoxia and hypercapnia, together with recurrent attacks of bronchitis, are possible precipitating factors.

The clinical features resemble closely those seen in emphysematous patients with chronic cor pulmonale. No mention is made of either systemic hypertension or cardiac pain in any of these patients. Yet in my second case these were the predominant features, the picture being in every other respect that of pulmonocardiac failure. It seems, therefore, that these findings can be correlated with the chest deformity. This was at least partially borne out by the necropsy findings, not only in this case but also in the first case, where the primary change appeared to be mechanical interference with the pulmonary circulation, leading to progressive enlargement of the right side of the heart. This caused kinking of the aorta against the spine, with eventual left ventricular enlargement, atheroma of the ascending and transverse aorta, and deformity and partial occlusion of the mouths of the coronary arteries. Thus it seems reasonable to postulate that the high blood-pressure in the second case was the direct result of the mechanical kinking of the aorta, which was so prominent at necropsy, although such kinking is said to play no part in these cases (Wood 1956). The chest pain was of cardiac type, and presumably due to myocardial ischæmia secondary to atheroma of the coronary arteries.

The report of a few cases is usually of little value, especially when, as in this series, specialised investigations have been kept to a minimum. But I think these four cases are worth describing. Pulmonocardiac failure is relatively uncommon, and may easily escape attention altogether. All four cases illustrate the seriousness of severe chest deformity, with its liability to cardiac and pulmonary embarrassment and early death, and draw attention to the need for early surgical intervention where this is practicable, or for expert orthopædic care in the child with chest deformity which is not amenable to surgery. Because of the part played by recurrent bronchitis in precipitating failure in kyphoscoliosis, intensive antibiotic therapy should be used to control rapidly any acute flare-up. Indeed, a strong case could be made out for the use of continuous antibiotic therapy in these cases.

Summary

Four cases of deformity of the chest are described. Two of them were fatal and the necropsy findings are discussed. In one case of pectus excavatum surgery was carried out successfully. In the fourth and mildest case physiotherapy was of value.

Because the outlook is serious in most of these cases greater attention should be paid to deformities of the chest.

REFERENCES

Abrahamson, L., Abrahamson, M. (1949) *Irish J. med. Sci.* **281**, 227.
Brown, A. L. (1939) *J. thorac. Surg.* **9**, 164.
Chapman, E. M., Dill, D. B., Graybiel, A. (1939) *Medicine, Baltimore*, **18**, 167.
Chin, E. F., Adler, R. H. (1954) *Brit. med. J.* i, 1064.
Hanley, T., Platts, M. M., Clifton, M., Morris, T. L. (1958) *Quart. J. Med.* **27**, 155.
Wachtel, F. W., Ravitch, M. M., Grishman, A. (1956) *Amer. Heart. J.* **52**, 121.
Wood, P. (1956) Diseases of the Heart and Circulation. London.

FŒTAL ERYTHROCYTES IN THE MATERNAL CIRCULATION

ALVIN ZIPURSKY
M.D. Manitoba
RESEARCH FELLOW IN DEPARTMENT OF PÆDIATRICS

ALAN HULL
B.Sc. Manitoba
RESEARCH ASSISTANT, DEPARTMENT OF BIOCHEMISTRY

F. D. WHITE
Ph.D. Edin., F.R.I.C.
PROFESSOR OF BIOCHEMISTRY

L. G. ISRAELS
M.D., M.Sc. Manitoba, F.R.C.P.(C.)
ASSISTANT PROFESSOR OF BIOCHEMISTRY

From the Faculty of Medicine, University of Manitoba, Winnipeg, Canada

Kleihauer et al. (1957) recently reported that the hæmoglobin of adult red cells in a fixed smear was readily eluted by an acid phosphate buffer whereas the hæmoglobin of fœtal cells was not. We have applied this observation to the detection of small numbers of fœtal cells in the blood of newly delivered women.

Venous blood was collected with ammonium-potassium oxalate as anti-coagulant, and diluted 1 in 3 with normal saline. Smears were made of this saline suspension, dried, and fixed in absolute ethyl alcohol for 2 minutes. After fixation and drying, the slides were washed for 90 seconds in citrate phosphate buffer (0·16*M* K_2HPO_4 and 0·18*M* citric acid, pH 3·4–3·6 at 37°C). They were stained with May-Gruenwald and then washed until practically no stain was visible to the naked eye. After drying, they were examined microscopically under low power. Fœtal cells appeared as pink-staining refractile cells in a field of erythrocyte ghosts (figs. 1–4).

In-vitro mixtures of fœtal and adult blood were made and smears prepared as described above (fig. 1). Arbitrarily, each smear was scanned for 2 minutes under low power. The numbers of fœtal cells seen in a 2-minute scan of smears of various dilutions were:

Fœtal cells/adult cells	No. of fœtal cells seen
1/25,000	2
1/10,000	7
1/5000	10
1/1000	21

When three adults were given 3, 5, and 15 ml. of compatible placental blood intravenously, the fœtal cells were demonstrated in the expected concentration in their blood (figs. 2 and 3). In the adult receiving 15 ml., the fœtal cells were still demonstrable 6 weeks after infusion.

The blood of 90 blood-donors (males and non-pregnant females) was examined. No fœtal cells were found.

The blood of 42 mothers, selected at random without reference to the blood-groups of mother and child, was examined on the 2nd to 6th day post partum with the following results:

No. examined (2-minute scan)	No. of fœtal cells	Estimated amount of fœtal blood in maternal circulation (ml.)
33	0	0·0
2	1	0·1
3	2	0·2–0·3
3	3–4	0·4–0·7
1	16	2·0–3·0

A fœtal erythrocyte in a maternal smear is shown in fig. 4.

The finding that 11 out of 42 (21%) postpartum women had fœtal cells in their circulation suggests that trans-

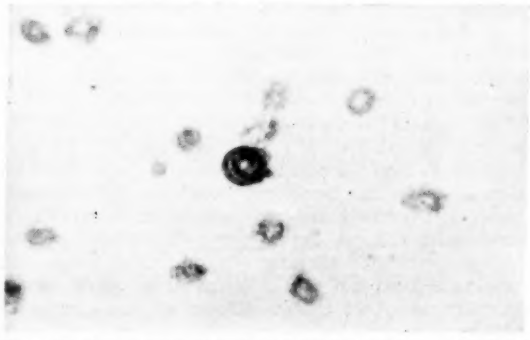


Fig. 1—In-vitro mixture of fœtal and adult red cells. The fœtal cell appears as a relatively intact refractile cell in a field of adult "ghost" erythrocytes.

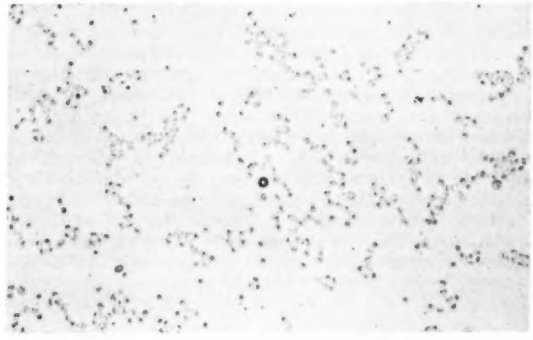


Fig. 2—Low-power photomicrograph of a fœtal cell in an adult, 3 weeks after injection of 15 ml. placental blood.

Fig. 3—High-power view of the same.

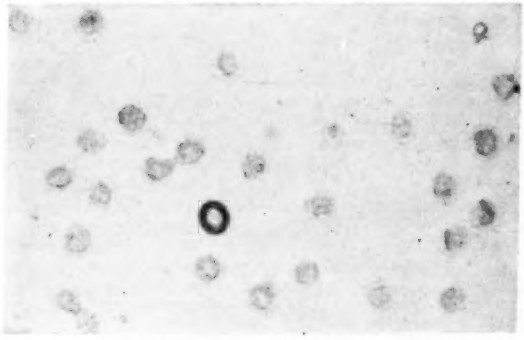


Fig. 4—Fœtal cell in a postpartum mother.

placental passage of fœtal blood is rather common. This finding, obtained by a relatively simple technique, is in agreement with those suggested by the more complex methods of Creger and Steele (1957) and of Hosoi (1958). This method has the advantage of not being dependent on the blood-groups of the mother or fœtus.

This study was aided by grants from the Playtex Park Research Foundation and the National Cancer Institute of Canada. We wish to express our thanks to Dr. B. Chown and Dr. J. Hoogstraten for help and advice.

REFERENCES

Creger, W. P., Steele, M. R. (1957) *New Engl. J. Med.* **256,** 158.
Hosoi, T. (1958) *Yokohama med. Bull.* **9,** 61.
Kleihauer, E., Hildegard, B., Betke, K. (1957) *Klin. Wschr.* **35,** 637.

A SIMPLE PORTABLE AID TO RESPIRATION

JAMES MACRAE
M.D. Glasg., F.R.F.P.S., D.P.H.
PHYSICIAN

R. V. WALLEY
M.D. Cantab.
DEPUTY PHYSICIAN

H. K. LUCAS
M.B.E., M.Ch. Orth. Lpool, F.R.C.S.E.
ORTHOPÆDIC SURGEON

HAM GREEN HOSPITAL, PILL, NR. BRISTOL

WHEN a patient's vital capacity is permanently small, his horizon is limited largely by the mass of mechanical equipment needed for artificial respiration.

So-called portable apparatus, such as the Monaghan cuirass respirator, is not easily manageable, and with batteries, it weighs as much as 150 lb. Glossopharyngeal breathing (Dail et al. 1955), if the patient can achieve it, is the ideal aid to respiration; but we have had many disappointments with it. Hence we have tried to devise simple equipment for artificial ventilation which would be truly portable as well as reliable.

A blower mechanism suggested itself—such as would have a high delivery of air and develop a pressure of about 15 cm. of water.

After experimenting with various types of small blower we found that these requirements are met by the Hoover 'Dustette' vacuum-cleaner. This instrument is small, (length 28 cm., height 11 cm., weight 2·45 kg.), and can be obtained commercially to work off a 12-volt battery. Since the dustette is used in reverse, as a blower, the collecting-bag assembly is removed and replaced by an airtight tubed aluminium alloy plate machined to fit the blower end of the machine. Plastic tubing ($^1/_2$ in. internal diameter) of suitable length (about 1 metre) is attached to the metal tube of the plate. The other end of the plastic tube is connected to a metal tube (10 cm. long) bent at right-angles so as to conform to the angle of the patient's chin. The other end of this metal tube has a short (6 cm.) length of plastic tube connected to it. This small piece of tubing acts as a mouthpiece and is readily replaceable.

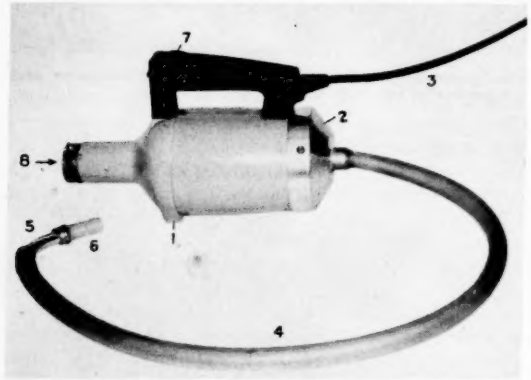


Fig. 1—Dustette blower respirator.

1. Dustette.
2. Aluminum plate.
3. Electric lead to battery.
4. Plastic tubing.
5. Angled metal tube.
6. Plastic tubing mouthpiece.
7. Dustette switch on carrying handle.
8. Direction of air-flow.

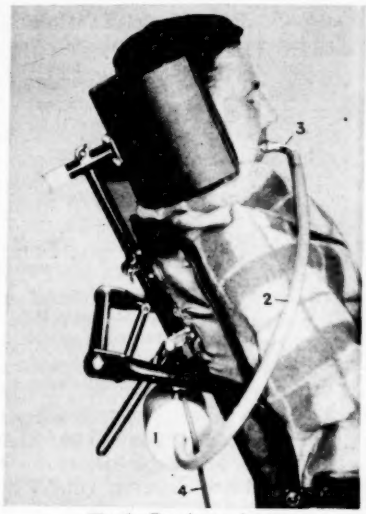


Fig. 2—Respirator in use.

1. Dustette.
2. Breathing-tube.
3. Metal angle-piece.
4. Flex to battery.

The mouthpiece is held by the patient's teeth, the blower is switched on, and inspiration can occur to any required depth simply by holding the mouthpiece loosely between the teeth and closing the mouth and nasopharynx. Biting the mouthpiece firmly permits expiration. These simple breathing movements have been mastered almost immediately by five of our patients who have vital capacities of about 300 c.cm. A humidifier does not seem to be necessary. The patients can readily control inspiration and vary its volume at will. "Vital capacities" of 1500 c.cm. are easily achieved. Comfortable artificial respiration by this method can go on for long periods, or, as is more usual with our patients, intermittent short intervals of "blower breathing" can be used to relieve the effort of breathing at low levels of vital capacity. With the blower equipment, talking is possible and expansion of the lungs is remarkably good. Our patients have come to trust the reliability of the blower respirator. Its small bulk allows long journeys in a wheel chair, and motor-car rides have for the first time become possible for these patients. Naturally, the improvement in their morale is substantial. The tubing is not unsightly and gives an impression of pipe smoking. The apparatus makes little noise and does not attract attention in public places. Patients cannot, of course, sleep or eat while using the blower.

One patient with a vital capacity of about 250 c.cm. was successfully taken 180 miles by ambulance and train using the "blower" intermittently on the train and wholly on both ambulance journeys. Another similar patient was perfectly happy with blower respiration before, during, and after an operation performed under local anæsthesia in an operating-theatre some distance from his ward.

To drive the dustette we have used a 12 volt 'Nife' battery of 20 ampere-hours' capacity. Fully charged, this battery will operate the blower continuously for as long as three hours at pressures of between 20 to 15 cm. of water, and the blower does not heat up during such a continuous run. The battery measures $44 \times 22 \times 19$ cm. and weighs 18 kg. It is readily accommodated beneath the seat of a wheel chair. The cost of the apparatus is very modest.

REFERENCE

Dail, C. W., Affeldt, J. E., Collier, C. R. (1955) *J. Amer. med. Ass.* **158,** 445.

Reviews of Books

Psychiatry in the British Army in the Second World War

ROBERT H. AHRENFELDT, formerly deputy assistant director of Army Psychiatry, Army Medical Directorate, War Office. London: Routledge & Kegan Paul. 1958. Pp. 312. 35s.

Dr. Ahrenfeldt states that his book has three main purposes: to record the work of Army psychiatrists in the care and treatment of the psychiatric Service patient, their contribution to solving problems of personnel-selection and proper use of manpower, and how their efforts resulted in a clearer appreciation of the importance of preventive psychiatry. His critical and explanatory account, not an official history but based on official documents, makes absorbing reading; for we are told not only how Army psychiatry developed but why the successive stages in its development took place. The scope of the problems to which Army psychiatry was applied is indicated by the chapter titles: personnel selection; officer selection; mental defect and dullness; disciplinary problems; treatment and disposal of psychiatric cases; forward psychiatry; problems of training and morale; and rehabilitation and civil resettlement of repatriated prisoners-of-war. Not only had great numbers to be dealt with, but the leading Army psychiatrists had to devise new administrative methods and to secure cooperation from the Army authorities, often in the face of considerable prejudice even among their medical colleagues. This readable book amply fulfils its author's purposes.

The Management of Emergencies in Thoracic Surgery

JOHN BORRIE, M.B.E., CH.M., F.R.C.S., F.R.A.C.S., thoracic surgeon, Dunedin Hospital, New Zealand. New York: Appleton-Century Crofts. 1958. Pp. 340.

THIS book reviews usefully the pathology, clinical features, and treatment of many thoracic surgical emergencies. These include injuries to the chest wall and pleura, empyema and lung abscess, postoperative complications, inhaled or swallowed foreign bodies, œsophageal fistula and rupture, strangulated diaphragmatic hernia, and cardiac wounds and arrest. Thoracic surgeons may disagree here and there with Mr. Borrie's views: for example, surgical drainage of lung abscesses has long been abandoned by most; and the photograph of how to fix an empyema tube shows well enough how not to do it. Nevertheless the book covers competently a field outside the scope of most surgical textbooks, and it should prove valuable both to general surgeons and to the junior staff of thoracic surgical units.

Leukemia

WILLIAM DAMESHEK, M.D., professor of medicine, Tufts University School of Medicine, Boston, Mass.; FREDERICK GUNZ, M.D., PH.D., hæmatologist, Christchurch Hospital, Christchurch, New Zealand. New York and London: Grune & Stratton. 1958. Pp. 420. £5 11s.

THIS book begins with a most interesting chapter on the growth of knowledge about leukæmia and the development of terminology and classification. The authors' own classification is sensible; they decry the currently fashionable use of "lymphoma", but are not very satisfied about the blanket use of "reticulosis". Information on the increasing prevalence of leukæmia and the work on ætiology are well reviewed; "some if not all forms of leukemia are essentially neoplastic", they think, and they are unimpressed by virus "propaganda". The "pathology of the leukemic cell" is being studied not only morphologically but also by histochemistry, which they think very promising. A chapter on the "course and special pathology as related to symptomatology" covers features common to most types of leukæmia, and then a separate chapter describes the features of the recognised forms of leukæmia including "myelomonocytic" (the so-called Naegeli form of monocytic leukæmia), Di Guglielmo's erythræmia, and multiple myeloma. The chapters on diagnosis properly emphasise that laboratory investigations have the last word, but the authors agree with those who think that newer methods such as phase-contrast and electron microscopy have done little to help differential diagnosis. They do not mount their own hobby-horses, and even myeloproliferative disorders are not given undue prominence. As regards therapy: "The evidence is by now overwhelming that present-day treatment of acute leukemia is capable not only of producing remissions and thus leading to prolonged periods of normal health, but actually to extend the total survival time".

This book is always balanced in its discussions—and there are real discussions, not just lists of other people's views. It is at the same time notably complete, taking account of all significant American papers and quite a lot of British and other European ones too. The illustrations are not excessive and are always apt to the text; a few colour plates show fields prepared from paintings. This work is a worthy successor to Forkner's classical text.

The Waking Brain

H. W. MAGOUN, PH.D., University of California School of Medicine, Los Angeles. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958. Pp. 138. 36s.

AT present the reticular system is much to the fore in neurological work, and this book is an account of some of the work done by Dr. Magoun and his colleagues in Los Angeles. The reticular system is thought to be a major and non-specific mechanism, lying centrally in the brain, which is able by its many interconnections to affect the function of all other parts of the central nervous system, and so of the body as a whole. It is thought, also, that the reticular system can raise or diminish the activity of other centres, and integrate their several activities. If this idea is correct the importance of the reticular system is obvious.

After a historical introduction, Dr. Magoun considers in turn the influence of the reticular system on the spinal cord, on reception of, and response to, sensory impulses, on neuroendocrine and visceral activity, on wakefulness and attention, and on cerebral cortical activity. From his own and his colleagues' work Dr. Magoun concludes that the reticular system grades the activity of other parts of the brain. Its influence is widespread, and it appears to be divisible into a more tonically operating lower part and a more cephalic component with the capacity for fractionated shifting influence upon focal regions of the brain. It seems that the reticular system is even involved in conditioned learning. This small, excellently produced, but expensive book will interest all neurologists.

Young Children in Hospital (London: Tavistock Publications. 1958. Pp. 103. 4s. 6d.).—This book by James Robertson is published as an accompaniment to the second of his films. Mr. Robertson has done much to encourage hospitals to humanise the care of child patients; but unfortunately his conclusions are presented here in a way which can lead to misapprehensions. Firstly, awareness of the possible dangers of separating mothers and young children should not be allowed to bring about a failure to put first things first: in acute illness the appropriate physical treatment must take precedence, for when life is in danger the primary psychological and physical needs coincide; and the behaviour which Mr. Robertson depicts and describes as typical of the young child in hospital may not be true of the acutely ill child. There is a widespread feeling that the psychological reaction to a stay in hospital on account of severe illness may differ from that of a well child separated from its mother. There is great need for research on this—as also on the psychological effect of physical illness in children who are cared for by their mothers. Illness has its psychological meaning for the child, whether or not the mother is present. This leads to the other potentially harmful implication—that "continuous" care by the mother can relieve the child of all anxiety, whether he be well or ill. Such a standard of care is beyond human attainment; yet, if this aim is set, mothers will try to reach it and will suffer correspondingly from a sense of guilt at their own failure. These criticisms do not amount to a plea against endeavours to relieve young children of anxiety by preserving the essential link with their mothers, but they do reflect the need not to underestimate the complexity of psychological reactions in sickness or in health.

Fungous Diseases and their Treatment (London: Butterworth. 1958. Pp. 256. 45*s*.).—Medical mycology, once the pretty toy of the simple skin doctors, now attracts more general interest. This book, edited by Dr. R. W. Riddell and Dr. G. T. Stewart, contains the contributions to a symposium held in London in 1957 under the ægis of the British Postgraduate Medical Federation. Prof. W. St. C. Symmers' chapter on pathological aspects of some cases of fungous infection seen in Great Britain is delightfully fresh and original. E. Drouhet, of the Pasteur Institute, reviews generally the therapeutic use of modern antifungal agents, and others discuss more limited applications. It is symptomatic of the rate of change that the therapeutic chapters will soon be out of date. Nevertheless, the editors are to be congratulated on producing a timely and stimulating book.

Symposium on Nuclear Sex (London: Heinemann Medical Books. 1958. Pp. 188. 21*s*.).—A meeting was held in London in September, 1957, during Prof. Murray Barr's visit to this country, so that workers in this country could have an opportunity of reviewing with him the notable developments in biology and medicine which have followed his discovery, with Dr. E. G. Bertram, in 1949 of a sex difference in the nuclei of cells. The papers read at the meeting and the discussions on them have now been published under the editorship of Dr. D. Robertson Smith and Dr. W. M. Davidson.

Poliomyelitis (Philadelphia: J. B. Lippincott. London: Pitman Medical Publishing Co. 1959. Pp. 684. 60*s*.).—The proceedings of the fourth International Poliomyelitis Conference, held in Geneva in 1957, have now been published. In his forword Dr. Morris Fishbein, chairman of the committee on publications, mentions as the conference's "centers of interest" vaccination, enteric viruses, and cultures of mammalian cells.

New Inventions

SERIAL TUNNEL FOR RADIOGRAPHY DURING OPERATIONS

RADIOGRAPHY during operations has been hampered by the difficulty of obtaining serial films without considerable disturbance to the operation field and the risk of introducing infection. The relatively simple cassette tunnel described here enables up to six serial films to be obtained without disturbing the surgical field; and with the modern four-valve transportable X-ray unit excellent films can be obtained.

The apparatus (fig. 1) consists of a tunnel 6 ft. 6 in. long and 2 ft. 3 in. wide corresponding to the size of a standard operation-table. The upper surface of the tunnel is made of lead plywood (1 mm. lead equivalent) except for an area of 12 in. × 10 in. or 15 in. × 12 in. which is made of 'Perspex' ($^1/_4$ in. thick) let in as an insert at the junction of the middle and upper thirds of the tunnel. The perspex window is decentred so that it lies two-thirds to the right of the midline when a 12 in. × 10 in. perspex area is used, but with a 12 in. × 15 in. window the widest part of the window lies across the table.

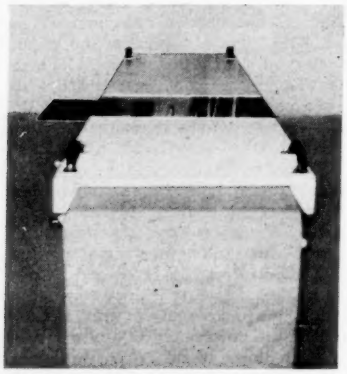


Fig. 1—Cassette tunnel in place on the operating-table: seen from the head end of the table with the linen runner in view.

A linen runner has six pockets sewn into it to carry 12 in. × 10 in. or 12 in. × 15 in. cassettes. The two pockets which lie at the head end of the tunnel contain two dummy cassettes.

The linen runner and the cassettes are loaded into the tunnel preoperatively, and the whole tunnel is placed on the operation-table before the operation. When the patient is carried on to the operation-table he is positioned so that the right hypochondrium lies over the perspex window and is centred before surgical cleansing, the first of the four cassettes being already in place beneath the window. A stationary grid is slipped into a slotted groove beneath the perspex window (fig. 2).

The films are withdrawn by hand-pulling on the linen runner from the head end of the table, and each cassette is indicated as being correctly placed by markings on the linen runner. A radiotransparent foam-nylon mattress covers the apparatus during the operation.

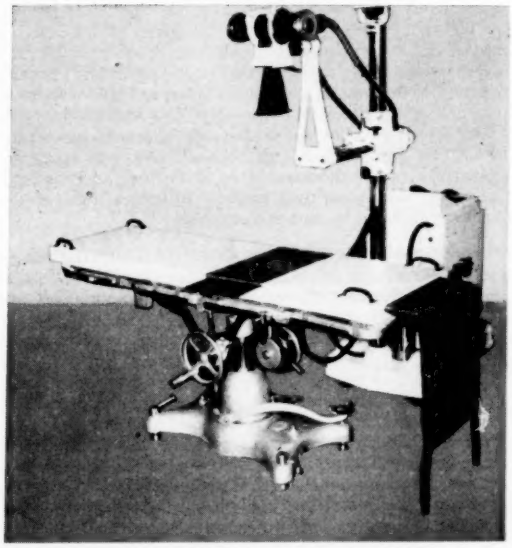


Fig. 2—Cassette tunnel in position, showing the perspex window and the grid in half-inserted position. The mobile unit is in place before the start of the operation.

Only the cassette which lies under the perspex window is exposed; the remaining exposed and unexposed cassettes are protected by the lead-ply upper surface.

In the past the quality of operative radiographic work has suffered from the limitation of output of the apparatus used; but, by the use of a mobile unit utilising full wave rectification, excellent films can be obtained.

If it is desired, especially in the apparatus with a 15 in. × 12 in. perspex window, 12 in. × 10 in. films can equally be used (e.g., for operative cholangiography) by inserting dummy wooden blocks into the pickets of the linen runners so that the 12 in. × 10 in. cassettes are displaced to the right side of each pocket and do not slip when the runner is pulled through.

The tunnel, mainly utilised for operative cholangiography, for which it was initially designed, is also completely satisfactory for splenoportography and other procedures which do not require rapid changing of the cassettes.

The apparatus is fairly easy to construct, and the hospital carpenter's shop can make it at extremely low cost.

Since the apparatus has been constructed and used, a somewhat similar tunnel has been described [1]; but the manner of obtaining serial films is more cumbersome and more time-consuming.

I am indebted to Mr. W. Trubshaw, F.R.C.S., for his assistance in developing and using this apparatus, and to Dr. Leon Morris, F.F.R., who built the prototype model for me.

ERIC SAMUEL
M.D. Lond., B.SC. Wales, F.R.C.S., F.F.R.

1. Rosenberg, A., Sampson, A. *Amer. J. Surg.* 1957, **93**, 873.

THE LANCET

LONDON 28 FEBRUARY 1959

Whose Responsibility?

ANYONE who investigates cross-infection in his hospital will come up against frustration; for who is to make the ultimate decision, whence is it to come? The word "responsibility" appeared no less than seven times in the last paragraph of the Nuffield Provincial Hospitals Trust's lucid and outspoken document on sterilising practice [1]—which said that the most important point made was the need to define responsibility.

Hard upon this comes the Medical Research Council working party's report on sterilisers, which we publish this week. Whereas the Nuffield publication was concerned with general defects and slipshod practices, too often unknown or unobserved by those who work in hospital, the emphasis of the M.R.C. report is on the complexity of the technique required in the proper loading and operation of autoclaves. These are processes in which one small lapse may bring failure. For example, when using a downward-displacement steriliser, one can defeat one's object simply by placing the drum on its bottom rather than its side. How many doctors or nurses know this? How many, indeed, know what type of steriliser their hospital uses; and, if they do, how many understand the principles underlying its use? Since the management of autoclaves is often left in the untutored hands of a hospital porter, it is not perhaps surprising that in the six hospitals studied by the Nuffield investigators 18% of ward and 12·5% of theatre equipment supposedly sterile was found not to be so; though in fact these failures were the outcome of many defects in the complex process. After reading the M.R.C. report we wonder whether the results would in fact be any better if the operation of the sterilisers were left in the experienced hands of the senior surgeon, who has the advantage of a rudimentary knowledge of bacteriology, physics, and chemistry. For the techniques of sterilisation call for special knowledge and for instruction, which is often lacking today because, as the report concludes, no one member of the staff is fully in charge.

Most urgent at this time in the fight against sepsis is the need to say where responsibility lies and then to ensure that it is accepted. Clearly it lies with the doctor; for, though much of the actual work of sterilisation and general hygiene necessarily falls to the nurses, the duty of seeing that things are properly done must remain with the doctors since they have the final responsibility for the care of patients. Moreover, though it is true that sepsis-rates may sometimes fall dramatically after the correction of a single glaring fault—in theatre ventilation, for example—they do not usually do so. There are many routes by which the ubiquitous staphylococcus may travel, and the best we can do is to impede as many as we can. This calls for perpetual awareness, persistent observation: indeed the battle can be won only by the continual application of intelligence—and seen thus is an exciting challenge. Who but the doctor has the width of training, the experience, and the variety of contacts to discover failures which can be of so many kinds? Thus he alone can be responsible. It does not suffice that we should demand better equipment or up-to-date accommodation; for all will be useless unless those who work in hospitals review their every action in Listerian terms, cultivating self-discipline to control themselves and courage to assert their standards.

Even failure by committee is our affair. Committee rule is a necessary part of what we consider to be free institutions, and it is also thought to be a prerequisite of cooperation. Nevertheless, as committees and sub-committees increase, responsibility diminishes until, by ever wider dispersal, it may virtually disappear. Sometimes, unconsciously, committees are positively used for this purpose, and "sharing responsibility" is no more than a euphemism for shedding the load. At other times they act with determination but fail to act together. Here is a simple example of which we have heard:

> The need to eliminate lysol or concentrated carbolic acid from wards and theatres is generally recognised. A committee set up to standardise methods and equipment within a group of hospitals, desiring to exclude all possibility of burns due to these dangerous chemicals, decided to take the step; it rightly recommended that their use in trays for the sterilisation of scalpel blades, scissors, and the like should cease. Next door, so to speak, the hospital committee on infection was sitting. Word reached them of the suggested change; but, after deliberating, they felt unable to approve it, because they knew of no solution, guaranteed to kill spores, with which to replace lysol. So the matter was left in the air pending investigations. Meanwhile, however, the suggested reform was quite properly discussed and explained on the distaff side, who, knowing nothing of the second committee's doubts, took appropriate action. Before long, therefore, a surgeon discovered his scalpel lying in a substitute solution whose sporicidal capacity had been questioned by bacteriological members of the infection committee. All the surgeons in that particular hospital had unwittingly submitted their patients to possible risk. Where did the responsibility lie?

The reasons why sepsis is increasing are various. One of them is psychological—the feeling among doctors that nowadays they have less say in the running of their hospitals. Others are diffusion of responsibility (through increase in the number of staff), frequent distraction (for it is hard to keep abreast of so many absorbing advances), the seductions of antibiotics, and perhaps some loss of the sense of mission. Putting simple things first, is it not the doctor's task to ensure that the people who work with him gain some knowledge of the elements of bacteriology—whether they are new theatre orderlies or the third kitchen hand? Unless he gives such instruction, he has only himself to blame when the new orderly places a dustpan and brush on top of the sterile glove-

1. Present Sterilising Practice in Six Hospitals. Nuffield Provincial Hospitals Trust. 1958. See *Lancet*, 1958, ii, 1359.

drum. The signs are that, in face of an enlarging threat to the safety of patients, this responsibility, both for policy and for detail, will be increasingly accepted. Such regional conferences as the two we reported on Jan. 3 and Jan. 31 are encouraging. But the day will be won only when the majority of the clinicians become aware of the implications of a life devoted to asepsis and the habits dictated thereby.

At the heart of the matter lies the surgeon—not only because his work is so intimately connected with asepsis, but because, being thus identified with it, his actions are an example to all. Today this example is too often deficient; and there is a certain rugged individuality about surgeons which makes them, as a class, somewhat unreceptive to suggestions of change. Feeling that somehow the septic hazards do not apply to them, some surgeons continue to stroll casually in and out of theatre premises ungowned, uncapped, unmasked, and shod in outdoor gear. And so long as they display such symbolic confidence, the attempt to regain asepsis will fall far short of what is possible and necessary.

Mycobacterial Tuberculin Sensitivity

THE term "non-specific tuberculin reactions" has been used for many years in veterinary practice to describe reactions to mammalian tuberculin that are not due to infection with mammalian *Mycobacterium tuberculosis*.[1] Commenting in 1954[2] on the work of Dr. CARROLL PALMER and his colleagues on the tuberculin reaction in man we suggested that "sensitivity that is not due to *Mycobacterium tuberculosis* would be better described as 'non-tuberculous', for the reactions could be due to specific sensitivity to other agents". Since then there have been further advances; and we agree with EDWARDS and PALMER[3] that neither "non-specific" nor "non-tuberculous" is adequate and that "it is obviously going to be necessary to develop a more precise terminology for identifying the sensitivity in terms of the sensitizing agent".

Cattle infected with mammalian mycobacteria give larger skin reactions to mammalian than to avian tuberculin; and this is the basis of the comparative test used to detect tuberculosis in cattle. Following work on the prevalence of the reactions in man to large and small doses of mammalian tuberculin and their possible significance,[3] the World Health Organisation research teams injected avian and human tuberculin simultaneously at different sites in more than 3000 persons in India.[4] In those sensitive to small amounts of tuberculin the human tuberculin produced, in general, larger reactions than the avian; but in persons sensitive only to large amounts of tuberculin the avian reactions were bigger. This aspect has been extended by KUPER,[5] who carried out similar comparative tests on healthy schoolchildren in two localities in South Africa. Contrary to the results obtained in the mixed adult and child population studied in India, the avian reactions were larger even in those who reacted to small doses of the antigen, as well as in those who reacted only to the larger doses. The evidence suggested, too, that sensitivity to avian tuberculin was acquired at an earlier age than sensitivity to human tuberculin. A group of tuberculous patients were, as might be expected from the previous studies in animals, more sensitive to human tuberculin. It seems that in certain areas sensitisation of man to mycobacteria other than the human and bovine types of tubercle bacilli may be widespread, and that the sensitising organism may be closely allied to the avian bacillus.

In man infections with mycobacteria other than the human, bovine, and avian types have been recorded widely in the United States. The photochromogen infections appear to be especially prevalent in the Mid-West and the non-photochromogens in the South-East States.[6] EDWARDS and PALMER[3] have carried out many comparative tests using the standard mammalian tuberculin P.P.D.-S and tuberculins prepared from photochromogenic (P.P.D.-Y) and non-photochromogenic (P.P.D.-B) mycobacteria isolated from patients with disease resembling tuberculosis.

At Battey State Hospital in Georgia, 173 patients were tested with P.P.D.-S and P.P.D.-B. From 28 of them, only the "Battey" type of non-photochromogenic mycobacteria (from which the P.P.D.-B was made) had been isolated; and in all but 7 the reaction to P.P.D-B was greater than to P.P.D.-S. The remaining 145 had human-type *Myco. tuberculosis* infections. Only 4 had greater reactions with P.P.D.-B. 5 patients with "Battey"-type disease gave no reaction at all to P.P.D.-S (5 T.U.); and 40 of the patients with human-type tuberculosis gave no reaction to 5 T.U. of P.P.D.-B. The group of tuberculous patients reacted to P.P.D.-S according to the expected pattern—very few had small reactions, and the peak of the frequency curve of induration was around 15–20 mm. The curve with P.P.D.-B was quite different, for 30% had no reaction and there was no peak at all. On the other hand, among the "Battey"-type group the curve with P.P.D.-B resembled that with P.P.D.-S among the tuberculous, and the curve with P.P.D.-S resembled that with P.P.D.-B. The result seemed to be a clear demonstration of reactions with homologous and heterologous antigens.

Similar studies were undertaken at Suburban Cook County Hospital, Illinois, with P.P.D.-Y and P.P.D.-S in patients with human-type tuberculosis and disease associated with photochromogens. Here the differences in reaction sizes were slight; but reactions with the homologous antigen did tend to be a little larger than those with the heterologous antigen. This was interpreted as indicating close antigenic similarity between human-type *Myco. tuberculosis* and the particular photochromogenic mycobacteria investigated. But the possibility that a high proportion of the patients excreting photochromogens had tuberculous infections in addition, and were sensitised by human tubercle bacilli, should be considered. It seems to be established that the photochromogenic mycobacteria can cause lesions in man; but it cannot be assumed that all the patients excreting these

1. Francis, J. Tuberculosis in Animals and Man: A Study in Comparative Pathology. London, 1958.
2. *Lancet*, 1954, *i*, 244.
3. Edwards, L. B., Palmer, C. E. *Amer. J. Hyg.* 1958, **68**, 213.
4. W.H.O. Tuberculosis Research Office. *Bull. Wld Hlth Org.* 1955, **12**, 85.
5. Kuper, S. W. A. *Tubercle, Lond.* 1958, **39**, 380.
6. Runyon, E. H. *Trans. Veterans Admin. Conf.* 1958, p. 288.

organisms have had pure chromogen infections. The "Battey" type of non-photochromogen appears to be similar to avian *Myco. tuberculosis* [7]; and infection with it might give some protection against infection with the human or bovine varieties. Thus, a group of patients with lesions associated with the "Battey" type might contain very few individuals who were also infected with mammalian tubercle bacilli. On the other hand, the chromogenic mycobacteria may predominantly infect those who already have damaged bronchi, and a group excreting these organisms might contain a high proportion already sensitised to mammalian tuberculin before the chromogens arrived. The inference of close antigenic similarity hardly seems justified on the present evidence.

EDWARDS and PALMER extended their investigation to comparative testing of Navy recruits—a very suitable group, for they are drawn from all parts of the United States. The frequency of reactions to P.P.D.-B varied from about 65% in lifetime residents of the South-East (where disease associated with non-photochromogenic mycobacteria seems most prevalent) to only 30% in those who had lived in the North-East. Reaction to P.P.D.-S also increased in frequency from north to south, the increase being entirely among those with reactions between 6 and 11 mm. in diameter. If reactions to P.P.D.-S equal to or greater than those to P.P.D.-B were assumed to be caused by infection with human or bovine type *Myco. tuberculosis*, and reactions to P.P.D.-S smaller than those to P.P.D.-B to be caused by infection with other mycobacteria, then the geographic variations in the frequency of small reactions to P.P.D.-S could be entirely accounted for by the variations in the frequency of non-mammalian-type sensitivity. When these small reactions were excluded, the frequency distributions of reactions to P.P.D.-S among recruits from different areas were all similar to one another, and also to the pattern found among tuberculous patients. EDWARDS and PALMER claim that these findings "constitute striking confirmation of the hypothesis that a varying proportion of the small, so-called 'positive' reactions to the 5 T.U. dose of tuberculin are not indicative of tuberculous infection".

Bone-marrow Grafts in Human Disease

MUCH interest has been aroused by reports in the Press [8 9] that 6 Yugoslav scientists who had been severely exposed to radiation had been sent for treatment to the Marie Curie Hospital in Paris, where marrow "grafting" was used for 5 of them. Apparently in an accident with an experimental reactor all 6 scientists received a radiation dose of neutrons and gamma rays regarded as large enough to prove fatal within a short time—probably more than 500r. The patients were sent to Paris last October; 5 of them were given injections of human bone-marrow taken from voluntary donors, and the 6th was "cured by normal methods". Of the grafted patients 1 died in November, but the 4 others recovered; after 3 weeks they were considered to be out of danger, in January they were convalescent, and on Feb. 14 they left hospital. The French physicians included Dr. HENRI JAMMET, head of the radio-isotope section of the Marie Curie Hospital. According to the *New York Times* [9] he said that the patients had received blood-transfusions and special diets rich in vitamins; he said too that, though the treatment had been successful so far, the patients would have to remain under observation for some time.

This treatment of radiation blood disease by infusion of normal bone-marrow cells is based on experiments on the treatment of leukæmia that have been going on for some time.[10 11] The principle is that a large dose of total-body irradiation is administered; the dose is large enough to kill off the leukæmic bone-marrow throughout the body and to reduce to a minimum the normal resistance of host tissue to a heterologous "graft"—isologous grafts are rarely possible in the treatment of human disease. After the irradiation normal bone-marrow cells obtained from donors with normal blood formation are administered intravenously. These injected marrow cells lodge in the normal marrow sites and under favourable conditions undergo mitosis and repopulate the patient's marrow and blood with normal cells; but, since they are cells from another individual, they will show characteristics, such as the blood-groups, belonging to the donor. Last year we reviewed the results of the few reported clinical trials of this treatment.[11] Most of the patients had leukæmia; some had aplastic anæmia but were not given preliminary irradiation. The results were not impressive, but most of the patients were very ill at the time. It was clear that immunological reactions of the host against the grafted cells, and also unexpectedly of the graft against the host, were likely to prove serious obstacles in the practical application of bone-marrow grafting.

THOMAS et al.[12] had treated 6 patients with leukæmia with total-body irradiation and subsequent marrow infusion, and they recorded two temporary "takes" of the bone-marrow graft. THOMAS et al. [13] have now reported results in 5 further cases of leukæmia treated in this way and describe a follow-up on 1 of the "temporary take" patients from the first group. This patient had lymphatic leukæmia; he survived for 8 months from the time of the original treatment, and he died of complications due to widespread staphylococcal infection even though the bone-marrow still contained many erythroblasts, granulocytes, and megakaryocytes that were apparently maturing normally. Of the 5 new patients, 4 died from overwhelming sepsis or hæmorrhagic bronchopneumonia 6–16 days after irradiation, without any evidence that the marrow infusion had been successful; in 3 patients the marrow was taken from an immediate relative—father, mother, sister—so as to ensure that the tissue was genetically related. The 5th patient has survived so far for 7 months, and her

7. Bogen, E. Quarterly progress report, Veterans Administration Study of Chemotherapy of Tuberculosis, 1958, vol. 13, p. 69.
8. *Times*, Feb. 16, 1959.
9. *N.Y. Times*, Feb. 17, 1959.
10. See *Lancet*, 1957, ii, 127.
11. *ibid.* 1958, ii, 132.
12. Thomas, E. D., Lochte, H. L., Jr., Lu, W. C., Ferrebee, J. W. *New Engl. J. Med.* 1957, **257**, 401.
13. Thomas, E. D., Lochte, H. L., Jr., Ferrebee, J. W. *Blood*, 1959, **16**, 1.

record is very interesting. This patient was a 16-year-old girl with acute blast-cell leukæmia; 95% of the marrow cells were abnormal. She was given a total-irradiation dose estimated at 325r. On the next day she was given an infusion of 3×10^9 marrow cells, the donor being the patient's sister whose only blood-group difference from the patient was in the Duffy group, the patient being Duffy A— and the sister Duffy A+. After treatment the patient was given the usual supportive treatment with fresh-blood transfusion, cortisone, and antibiotics, and she successfully combated the post-irradiation sepsis that appeared. On the 36th post-irradiation day the bone-marrow was normal, and the patient was well on the way to recovery. By means of the technique of JONES and SILVER [14] it was shown that the donor red cells of the Duffy A+ type gradually disappeared from the patient's blood, and by the 90th day after irradiation the patient's circulating red cells were all of her own original type. From this THOMAS et al. conclude that the transplanted marrow was " no longer functioning, at least in terms of red cell production ". On the 128th day blast cells again appeared in the peripheral blood, and on the 134th day marrow aspiration showed 20–30% undifferentiated blast cells in an otherwise normally active marrow. The patient was given treatment with mercaptopurine and steroids and was well on the 203rd day.

THOMAS et al. discuss the many difficult problems that arise in treatment with whole-body irradiation and bone-marrow infusion. One serious problem is the liability to infection that the total-body irradiation causes, and there is evidence that, even when the marrow graft is successful, so much lymphoid tissue is destroyed that the result is " an immunological cripple with an inadequate lymphoid system incapable of reacting effectively to outside antigens, bacteria, etc.". Experimental work has suggested that the addition of spleen cells to the marrow infusion might overcome this difficulty, but so far this expedient has not been tried in man. Another problem is the correct range of dose for effective total-body irradiation and how it should be given. THOMAS et al. think that the 400–600r range is dangerous and give reasons for limiting the dose to 200–300r. They are entirely dissatisfied with present methods of administering total-body irradiation, and they suggest how " appropriate arrangements " could be made to ensure uniform exposure; they point out that experiments with irradiation of mice, which are structurally different, should not be expected to provide a guide to what is needed in man.

One difficulty in assessing the value of bone-marrow grafts is the formidable complication introduced by working with cases of leukæmia. For this reason the accident to the Yugoslav scientists, lamentable though it was, may provide us with valuable information, because the accident exposed persons with normal hæmopoiesis to total-body irradiation. The French workers may be able to answer important questions. Can they say how long the marrow grafts survived? Do these grafts simply survive in the irradiated patients until their own cells recover and take over hæmopoiesis once more? In THOMAS's surviving patient the marrow graft did not apparently survive beyond 90 days; and it will be interesting to learn whether the grafts have persisted in the Yugoslav scientists, who have already passed the 90-day mark. We hope that our French colleagues will publish the details of their treatment and of the short-term and long-term results.

14. Jones, A. R., Silver, S. *ibid* 1958, **13**, 1.

Annotations

RUSSIAN RESEARCH ON HYPERTENSION

BECAUSE of political and language barriers that divide the world the Western student cannot easily keep himself informed on medical progress in Russia, and a comprehensive review of Russian work on an important subject is as rare as it is welcome. A review on arterial hypertension by Simonson and Brožek [1] is valuable in that it not only covers over two hundred articles, few of which would be readily accessible to the Western reader, but also shows how widely the Russian approach to this important problem differs from our own. The authors attribute this difference largely to the tremendous impact of Pavlov's work and concepts on all biological and medical thinking in a country where deference to authority is axiomatic.

In brief the prevailing view is that essential hypertension is a disease of the central nervous system in which psychogenic disturbances of cortical inhibitory function increase the excitability of hypothalamic vasomotor centres, causing first transient and then persistent increase in arteriolar tone. Cardiac, renal, and endocrine involvement are believed to be secondary, and important only in the later stages. This concept is of course not new, nor is it limited to Russia. But, whereas in the Western world attention has been concentrated mainly on humoral factors, in Russia the emphasis has been on nervous agencies. Since the cause of essential hypertension (by far the commonest form of the disease) remains unknown, neither party has any cause for complacency. In the laboratory animal hypertension of varied degree and duration has been provoked by cerebral trauma, by electrical excitation of the brain, by strong (e.g., acoustic) stimuli, and, according to several Russian workers, by conditioned reflexes. These findings are suggestive and of great interest. So also is the fact that constriction of the renal arteries causes a much more convincing and complete replica of the disease seen in man. But just as the latter does not prove the renal origin of essential hypertension, so the former is not enough to establish the neurogenic theory.

What is now needed is direct evidence from man, and to be convincing this must show that the postulated cause is regularly present in hypertensive disease and precedes its onset, and that removal of the cause will abolish early established hypertension. Where the suspected cause is a functional nervous or psychological disturbance, satisfactory direct evidence is not easy to obtain. " Stress " is a fashionable but vague word, difficult enough to define, let alone measure; while even the estimation of blood-pressure by the usual indirect methods is open to gross subjective and objective errors, and a reading gives at best only a momentary glimpse of a continuously varying level. These factors are particularly important where a single observer attempts to measure the immediate effect of psychological " stress " on the blood-pressure. In

1. Simonson, E., Brožek, J. *Ann. intern. Med.* 1959, **50**, 129.

such circumstances a pharmacologist—that is, someone trained to assess the effect of a variable on a body function—would require that the "stress" should be defined in the clearest possible terms, that the pressure should be measured either mechanically or by an independent observer, and that the design of the experiment and the results should be acceptable to a competent statistical referee. These are difficult precautions to observe in this kind of clinical research; and most work in this field, from whatever source, fails to carry conviction because it has not been so controlled. This means, not that the neurogenic hypothesis is disproved, but simply that a great deal more work is necessary; and the present review provides an admirable starting-point for fresh efforts.

In treatment Russian practice does not differ materially from that in other countries, but two novel measures may be mentioned. One is the use of oxygen to relieve cerebral symptoms such as headache; the duration of the relief is not stated. The other is sleep therapy, which is also used in other diseases. Sleep is induced by such drugs as amylobarbitone sodium and chloral hydrate, and is maintained for up to twenty hours a day for twenty to twenty-five days. Several reports claim improvement lasting for many months, but only, unfortunately, in the early stages of the disease.

THE DESIGN OF CHAIRS

WHEN, in 1741, the professor of medicine at Paris published a book for the title of which he coined the word "orthopædics",[1] he included two illustrations showing a person sitting in a "good" and a "bad" posture. In more recent and more scientific times, the naval and military authorities in the 1939–45 war sought expert anatomical and anthropometric advice on the construction of certain special seats—for instance, those used by gunlayers.[2] Now the British Standards Institution has published a report on the scientific principles involved in the design of office chairs and tables.[3]

The report makes it clear that there can be no single design for an "ideal" office chair. Floyd and Roberts cite Akerblom as saying "a good chair is one which permits of as many good postures as possible being adopted". The seat of a chair, they suggest, should be such that the body-weight is transferred mainly through the ischial tuberosities. The weight could be placed more on the ischial, and less on the thigh, areas by shaping or excavating the seat—as in the kidney-shaped "ploughman's seats". But such patterns do not allow for great variations in the size of the buttocks between one individual and another. The seat should rather be substantially plane, and fairly hard. Materials which yield, far from being more comfortable, will distribute the weight to soft tissues, causing ischæmia and hypoæsthesia. In general, a chair is of optimum height when even a short person sitting on it can place his feet flat on the ground with his knees flexed to 90°. Taller occupants will need to flex their knees more, but will still be comfortable as regards weight transmission and the position of the hip-joints; but unfortunately such people will, if the chair is too low, need to maintain exaggerated lumbar lordosis to sit upright, and will therefore be uncomfortable. For this reason a universally comfortable chair must probably be of variable height. The optimum position for a back-rest is in the lumbar region; it should support the spine at this level in a position short of full flexion, and should not restrict movement of the spinal column or of the arms. A complete support for the whole back is therefore excluded.

The chief gains from such careful studies as this are likely to be decreased fatigue and higher work output among office workers and benchhands. But automobile designers and theatre proprietors, as well as business executives, may be prepared to sponsor research on this subject, thus following in Floyd and Roberts' footsteps—if that is indeed the correct phrase for such a sedentary topic.

1. Nicolas André. Sur l'Orthopédie. Paris, 1741.
2. Darcus, H. O., Weddell, A. G. M. *Brit. med. Bull.* 1947, **5**, 31.
3. Floyd, W. F., Roberts, D. F. Anatomical, Physiological, and Anthropometric Principles in the Design of Office Chairs and Tables. London: British Standards Institution. 1958. 5*s*.

FUNCTION OF THE TEMPORAL LOBES

IN the past decade the functions of the temporal lobes have largely ousted those of the frontal areas as a centre of neuropsychiatric interest. This is understandable. The evidence from both man and animals suggests that the temporal regions of the brain play an important part in the organisation of conscious behaviour, particularly in relation to emotional experiences and memory.

The evidence is not wholly new. Much of it was known to Hughlings Jackson nearly a hundred years ago. Recently, however, many psychologists (and some psychiatrists) have once more become aware of the brain as the organ of mind, and of the importance of establishing a cerebral substrate for emotion. Advances in neurosurgery and electrodiagnosis also have provided greater scope for studying localised brain function. These factors are doubtless in part responsible for the renewed interest.

In animals a profound alteration in behaviour may follow bilateral temporal lobectomy. Monkeys are described as more tame, less aggressive, and less fearful—to such a degree that they may show no apprehension of dangers to life. Such descriptions, however, may not uncover the real nature of the changes, which certainly need further study. The picture of a lobectomised postoperative monkey readily handling a snake—which normally produces a brisk fear and avoidance reaction—almost suggests a perceptual or at least agnostic difficulty.

In man severe damage to both lobes may produce a gross defect of memorising, with reduction of the effective memory span to only a few minutes, as in severe Korsakoff's psychosis. Lesser degrees of damage may give rise to an epileptic focus whose overt discharge produces a psychomotor attack with automatic behaviour and amnesia. Diverse visceral and emotional changes may also form the aura or the content of such fits. Besides the very common epigastric aura, alterations in heart-rate, vasomotor and pseudomotor state, respiration, and bowel and bladder function, and manifestations of fear, anger, anxiety, depression, and (more rarely) elation can all occur. Moreover the background personality may be altered even between attacks, so that a psychopathic or even psychotic picture emerges. Increasingly what used to be called the epileptic personality is being recognised as the "temporal-lobe" personality. These points are well illustrated by Brown et al.[1] in a study of 25 such cases. All of them underwent surgical excision of their temporal-lobe foci, and the results left no doubt that the psychomotor element of their attacks did in fact arise in the activity of temporal-lobe tissue. Bingley [2] has fully

1. Brown, I. A., French, L. A., Ogle, W. S., Johnson, S. *Medicine, Baltimore*, 1956, **35**, 425.
2. Bingley. T. *Acta psychiat., Kbh.* 1958, **33**, suppl. 120.

reviewed the mental changes in temporal-lobe epilepsy, and has also described the more subtle personality changes —a curious perseverative tendency or mental adhesiveness for which the term " ixophrenia " has been coined.

As in epilepsy arising at other sites, the march of events in individual temporal-lobe fits may give information about the functional organisation of the area. An analysis by Stevens [3] suggests pathways of election, either anatomically or physiologically determined, for the passage of epileptic discharge. Thus an initial gastric sensation usually leads on to an unpleasant emotional state with fear or anxiety prominent; while a feeling of sorrow or despair tends to follow a feeling of strangeness or unreality, which itself is often preceded by specific visual distortion. The common association of visceral with emotional activity detected in this and other studies certainly confirms the view—expounded in the James-Lange theory, for example—that these two aspects of behaviour are closely linked.

Some of the manifestations of lesions in the temporal-lobe area, both in animals and in man, are similar to those of lesions in certain parts of the frontal lobes and in the hypothalamic region. A Korsakoff-like memory defect is a striking example. The evidence begins to suggest that a unified cerebral mechanism or group of mechanisms is concerned with memory and emotion; that this mechanism involves parts of the hypothalamic nuclei, the temporal lobes, and the medial frontal cortex; and that lesions in any of these regions may produce some similar symptoms —though the total picture may differ according to the region affected. Such observations suggest that Papez's [4] amply confirmed postulate of the limbic system as the neurological substrate of emotion may need extending to some aspects of memory also: which is perhaps not surprising in view of the close association of learning and emotion.

RELATION OF POTASSIUM DEPLETION TO MUSCULAR PARALYSIS

POTASSIUM depletion may arise in various different circumstances—for instance, in cases of chronic diarrhœa, vomiting, or gastrointestinal drainage, diabetic ketosis, over-production of aldosterone, or over-treatment with mineralocorticoids such as deoxycortone, or after long-continued administration of such diuretics as mersalyl and chlorothiazide. Severe loss of potassium from the body can lead to muscular weakness or actual paralysis, but the precise relationship between these two states has proved hard to define. Thus, Zierler and Lilienthal [5] state that " it requires the most strenuous emphasis that muscular weakness does not inevitably follow lowered concentrations of potassium in the serum ". In fact, the overall coincidence may be less common than the absence of it [6]; and Schwartz et al,[7] after analysing balance studies on patients with potassium depletion, concluded that the electrocardiographic findings are consistently related neither to the total potassium deficit nor to the serum-potassium level. An accompanying acidosis seemed to protect the patient from showing the electrocardiographic evidence of potassium lack, although potassium depletion per se induces extracellular alkalosis.

Some progress towards understanding the relationship between potassium deficiency and muscular paralysis has been made by Offerijns et al.[8] in Amsterdam. They studied the effect of low levels of potassium, both extracellularly and intracellularly, and of insulin on the contraction of isolated rat diaphragms, and found that potassium deficiency—extracellular or intracellular or both—did not cause paralysis of the muscle. In man, too, a potassium-free diet, continued long enough to reduce the total body-potassium by 28%, failed to produce muscular paralysis.[9] Yet when the Dutch workers added insulin to the isolated diaphragm of rats fed on a potassium-free diet and suspended the diaphragm in potassium-free Tyrode solution, muscular paralysis set in; the paralysis could be overcome by adding a small amount of potassium chloride to the bath fluid. Here again, a parallel can be drawn to studies on man. Thus Black and Milne,[10] using a potassium-free diet, induced a state of potassium depletion, judged by the serum levels and subsequent retention of potassium comparable to that following severe diabetic ketosis; and yet there were no serious clinical disturbances.

In a diabetic under treatment for ketosis with much glucose and insulin, Holler [11] noted severe muscle paralysis, and such observations have been repeated by others. Atchley et al.[12] were the first to show by metabolic balance studies that acute insufficiency of insulin induced a rapid preferential loss of intracellular potassium, and the same process in reverse was demonstrated by Nabarro et al.[13] in the first hours of insulin treatment of ketotic diabetics. Thus, the additional factor of the sudden restoration of insulin to the ketotic diabetic depleted of potassium seems to render him particularly liable to hypokalæmic paralysis, just as in the rat-diaphragm experiments. Insulin permits the transfer of potassium into cells and into glycogen.[14] Frankel et al.[15] suggest that the hyperglycæmia of some cases of diabetic ketosis with so-called insulin resistance may be due as much to rapid intracellular potassium depletion with blocked glycogenesis as to lack of insulin. This would be hard to confirm, because potassium salts are not normally administered to patients with severe diabetic ketosis until they have passed the phase of insulin resistance and the serum-potassium is falling. Earlier the serum-potassium may be high despite a gross potassium deficit, and thus the administration of potassium initially is hazardous. But normal rats kept on potassium-deficient diets for many days may have diabetic glucose-tolerance curves and very low levels of glycogen in liver and muscle.[16]

Insulin is one factor with a pronounced effect on the incidence of muscular paralysis in states of gross potassium depletion, just as insulin can induce paralysis in patients with familial periodic paralysis who have no potassium deficit. Other factors are the levels of calcium, magnesium, sodium, and hydrogen ions. Four volunteers [9] found that the symptoms of experimental potassium depletion were much more prominent in the presence of acidosis or while sodium was restricted; and Engbaek [17] showed that raised levels of calcium and magnesium could depress the excitability and contractibility of muscle.

3. Stevens, J. R. *Neurology*, 1957, **77**, 227.
4. Papez, J. W. *Arch. Neurol. Psychiat.* 1937, **38**, 725.
5. Zierler, K. L., Lilienthal, J. L. *Amer. J. Med.* 1953, **15**, 829.
6. Tarail, R., Hacker, E. S., Taymor, R. *J. clin. Invest.* 1952, **31**, 23.
7. Schwartz, W. B., Levine, H. D., Relman, A. S. *Amer. J. Med.* 1954, **16**, 395.
8. Offerijns, F. G. J., Westerink, D., Willebrands, A. F. *J. Physiol.* 1958, **141**, 377.
9. Fourman, P. *Clin. Sci.* 1954, **13**, 93.
10. Black, D. A. K., Milne, M. D. *Lancet*, 1952, i, 244.
11. Holler, J. W. *J. Amer. med. Ass.* 1946, **131**, 1186.
12. Atchley, D. W., Loeb, R. F., Richards, D. W., Benedict, E. W., Discoll, M. E. *J. clin. Invest.* 1933, **12**, 297.
13. Nabarro, J. D. N., Spencer, A. G., Stowers, J. M. *Quart. J. Med.* 1952, **21**, 225.
14. Fenn, W. O. *J. biol. Chem.* 1939, **128**, 297.
15. Frankel, M., Groen, J., Willebrands, A. F. *Arch. intern. Med.* 1947, **80**, 728.
16. Gardner, L. I., Talbot, N. B., Cook, C. D., Berman, V., Uribe, C. *J. Lab. clin. Med.* 1950, **35**, 592.
17. Engbaek, L. *Acta pharmacol.* 1948, **4**, 1.

Special Articles

THE RESULTS OF INGUINAL HERNIA REPAIRS
A PROBLEM OF ASSESSMENT

A. J. MARSDEN
M.B. Lpool, F.R.C.S.
RESEARCH ASSISTANT, UNITED LIVERPOOL HOSPITALS

"IT is difficult to exaggerate the importance of the ordinary inguinal hernia to the community, since it is a disability which affects an enormous number of able-bodied people, and is therefore probably of even greater economic importance than cancer." It was with these words that Keynes opened a discussion on inguinal hernia at the Royal Society of Medicine in 1937. Inguinal hernia *is* important, and it remains a problem. Every discussion on the operation is preceded by expressions of amazement at the variations of technique which continue to appear in medical journals, and at the lack of reliable information about the comparative value of the different procedures.

No-one now doubts the value of Bassini's (1890) suggestion that the sac should be excised at the internal ring, although some (including myself) occasionally follow Kocher (1903) and invaginate the sac through the ring. No-one now doubts the importance of preserving the normal fascial and muscular relations of the spermatic cord where these have not been stretched or damaged—as in children. Beyond this, however, there is no agreement.

At the 1937 meeting of the Royal Society of Medicine Ogilvie led the attack on the traditional view that some form of strengthening of the posterior wall of the canal is necessary in adults—both young and old. He pointed to the many recurrent herniæ which were undoubtedly the result of damage to the posterior wall by the method of repair. Max Page's studies (1934) of the results of inguinal-hernia repair had already produced considerable dissatisfaction with the traditional methods, and the writings of Edwards (1943a) and Lytle (1945) established a more conservative approach to inguinal hernia in younger adults. Edwards pointed out that 75% of recurrent inguinal herniæ followed a Bassini-type operation, and condemned this technique. Farquharson in 1955, on the other hand, used the same finding *in favour* of the Bassini operation, claiming that this is the technique which is by far the most commonly used, and that the figures therefore indicate a relatively low recurrence-rate.

The Problem

Though there is no lack of published results of the various techniques of repair, these have rarely been presented so as to allow a fair comparison. Doran in 1957 made one of the few attempts, using "random selection" of cases in accordance with statistical requirements; but his series was very small, and it is doubtful whether his method could be applied widely enough. With such rare exceptions, results have been assessed on widely differing criteria; whereas Max Page (1934) in 206 cases repaired in the main by the Bassini technique found 47 recurrences, Hoguet and Coley (1918) in 3725 cases repaired by the Bassini method, found only 14.

In 1951 in this department we set out to discover the results of hernia repair in the Liverpool region. After a pilot survey at a large regional hospital (Whiston) the main scheme was carried out in the United Liverpool Hospitals. All inguinal herniæ repaired in males of 16 and over were registered and reviewed one year and three years after the operation. The results of the first 1000 cases have now been published (Marsden 1958); and, though the investigation has not given a definite answer to the question which is the best technique of repair, it has displayed the difficulties of assessing various methods of repair and indicated how these difficulties might be overcome.

The Difficulties

The difficulties of compiling comparable statistics of the results of inguinal-hernia repair can be divided into four groups.

The Patient

It is quite unusual to find published results separating the different types of inguinal hernia, and yet this is essential if statistics are to be comparable. In our cases the recurrence-rate after the repair of primary direct herniæ has been over half as much again as after the repair of oblique ones, whilst the repair of secondary (recurrent) herniæ has yielded a recurrence-rate three times that of the direct. In presenting results recurrent herniæ should be excluded completely as being too variable in type to allow accurate comparison. Primary oblique and primary direct herniæ must be presented separately. The combined oblique and direct hernia—the pantaloon type—should probably be classified with the direct group.

I have found no series, apart from our own, which attempts to divide the cases according to the degree of damage to the fascia and muscles of the inguinal canal, the patient's musculature, and his obesity. This is not easy, since judgment of physique is never exact. Nevertheless, at operation one can divide cases into three categories:

1.—Patients with apparently normal muscles, in whom the surgeon would be particularly disappointed to see a recurrence.

2.—Those with weak, damaged or heavily fat-infiltrated muscles in whom the surgeon is pessimistic about the success of his repair.

3.—The remaining intermediate cases.

The results for the three categories must be separated. There are, of course, many obvious difficulties with so simple a scheme. An important factor, for example, is the height of the insertion of the conjoint tendon which affects the apposition of the tendon to the inguinal ligament (unless a relieving incision is made). Cases of high insertion probably belong to the second category.

The Surgeon

Not only are there many variations in basic technique, but often supplementary procedures are used—a "Tanner slide" (1942), a narrowing of the internal ring, or a Bracey (1956) fascia-lata incision—without this being mentioned in the printed account. Much worse than this is a lack of knowledge even of basic technique (and even of type of hernia) due to inadequate records. House-surgeons are often unable to write an adequate description of the operative procedure, sometimes abandoning the struggle with the statement "hernia repaired". The information is only complete when the surgeon has himself written or dictated the operation notes.

In the United Liverpool Hospitals series most repairs were performed by registrars who move once a year from one surgical team and hospital to another. A registrar usually adopts the technique favoured by his team, with the result that, over the years, most techniques are tried by most of the registrars, thus eliminating the variable factor of the individual surgeon's skill. Ideally, of course, individual series of operations by surgeons of acknowledged skill should be the basis for comparison.

The Strain

We have found that the time of "getting up" and of a man's return to work and the nature of his work had no significant effect on hernia recurrences. Undoubtedly, a high proportion of men attending surgical clinics with recurrent herniæ are heavy manual workers, but this is because they cannot work satisfactorily wearing a truss. Sedentary workers, when their herniæ recur, often get a truss from their doctor without returning to hospital. Probably the greater strain of heavy

work is balanced by the better musculature of the heavy manual worker. Farquharson (1955) advanced the view that the work after hernia repair is relatively unimportant as regards recurrence.

The period of time between the repair and its review is, however, of great importance. My study of a series of recurrent herniæ (1958) showed that in only 85 out of 230 cases was the patient aware of the recurrence within the first year after operation; and even after three years in only 114 cases was the recurrence obvious to the patient. No doubt, a surgeon would have detected a considerably higher proportion of recurrences at these times, but in any series the recurrence-rate will rise with the passage of years (Block 1933, Burdick 1937, Moloney 1948, 1958). Grace and Johnson (1937) suggested three to five years as a serviceable period. For comparable statistics the time of follow-up must certainly be standardised; but circumstances may force one to accept three rather than five years.

The Examination

Harold Edwards (1943b) has written that " one of the most important variants [affecting the statistics] is in the criteria of recurrence adopted. A small though definite bulge after operation may be discounted by some—and this will reduce the recurrence figure by 50% (Grace and Johnson 1937) ". Of Max Page's 47 policemen with recurrent herniæ no fewer than 12 were at full work without the aid of a truss, illustrating the disparity between the anatomical and the symptomatic results of a repair. In the Whiston series several of the men examined ten to thirteen years after the repair had their attention drawn to a small local bulge. Almost all of them asserted that this had appeared soon after their operation and had not grown bigger. In the United Liverpool Hospitals series a group of 81 men had a " small but definite bulge " at the one-year examination. Two years later only 6 of these had to be classed as definite recurrences. I agree with Grace and Johnson that a bulge is not a recurrence unless a later examination (usually after six months) shows deterioration.

There are various reasons for the unimportance of a bulge. Where the external oblique has been sutured behind the cord, so that the internal and external rings are approximated, there is often a vascular thrill in the cord on coughing; and this may simulate a small sac very closely, especially if there is a varicocele. After this type of repair a slight protrusion at the site of emergence of the cord in no way indicates a weakness. Deterioration of the inguinal musculature with the passage of years may also lead to a small or even large diffuse bulge—but this is not a recurrence. Finally, a small incompletely reducible swelling is sometimes found after operation at the pubic end of the canal: this enlarges on straining but remains symptomless and usually unknown to the patient for years, if not indefinitely.

A recurrence, then, is a weakness in the operation area necessitating a further operation or the provision of a truss. It is a failure of the operation and does not include slighter degrees of weakness—the significance of which is still controversial.

Doran (1958) recently analysed the enormous variations in follow-up statistics resulting from inefficient follow-up. Published figures range from Hoguet and Coley's series of 3725 cases with only 14 known recurrences in which less than two-thirds of the patients were actually traced and only a minority of these examined, to O'Connor's (1940) series of 103 cases, in which all but 19 patients (who had died or had left the district) were examined and found to be free from recurrence. It is, of course, difficult to get these patients to attend for follow-up examination, since so many of them are working men; but this difficulty can be partly overcome by eliminating from the series men living far from the surgical centre, those who have died or developed a chronic illness before their review was due, and those untraceable by the postal authorities or local executive council. The previously agreed elimination of such cases would not affect the value of the series for comparative assessment of the recurrence-rate. In the United Liverpool Hospitals series an 82% attendance for the three-year examination has been achieved, despite the large proportion of seafaring patients. I agree with Doran that a high-efficiency follow-up at three years is preferable to a less efficient one at five years.

There is nothing new about these pitfalls and difficulties: during the past twenty-five years Block, Burdick, Grace and Johnson, Edwards, Moloney, Farquharson, Doran, and no doubt many others, have laid stress on one or more of them. The time, surely, has come to implement their suggestions.

Solution

To make published results comparable I suggest the following set of rules.

1. The series must include *all* primary inguinal herniæ in males of 16 years or over which are repaired by the particular surgeon during a given period, with the exception of patients who are ill, dead, distant, or untraceable at the time of the follow-up.

2. The operation records must be adequate, recording the type of hernia, the technique of repair, the suture material used, and the prognosis based on an examination of the musculature at operation.

3. The examination must be personal, performed at a time not less than (and as near as possible to) three years after operation. At least 80% of patients must be examined, and further information about the others should be obtained from their doctors.

4. A repair should not be classified as a failure unless a further operation or a truss is necessary; but any doubtful case must be seen again at a time not less than six months later.

5. The results must be presented in such a way as to show a clear division between oblique and direct herniæ, and also between the three groups of varying musculature.

At present it is impossible to prove that a theoretical improvement in technique—such as a Bracey incision—is worth while, for there is no standard by which the modified operation can be assessed. It is impossible even to be sure that what is commonly called the Bassini technique is preferable to the Wyllys-Andrews methods. If the above rules are followed a dozen competent surgeons will be able to tell us in ten years which are the best ways to repair different types of inguinal hernia.

Summary

It is suggested that results of inguinal-hernia repair could be considerably improved if individual series were presented in such a way as to allow comparison of one with another. A basis for such standard presentation is put forward.

REFERENCES

Bassini, E. (1890) *Arch. klin. Chir.* **40,** 429.
Block, W. (1933) *ibid.* **175,** 607.
Bracey, D. W. (1956) *Ann. R. Coll. Surg. Engl.* **19,** 383.
Burdick, C. G., Gillespie, D.H.M., Higinbotham, N. L. (1937) *Ann. Surg.* **106,** 333.
Doran, F. S. A. (1957) *ibid.* **146,** 957.
— (1958) *Lancet*, i, 480.
Edwards, H. (1943a) *Proc. R. Soc. Med.* **36,** 185.
— (1943b) *Brit. J. Surg.* **31,** 172.
Farquharson, E. L. (1955) *Ann. R. Coll. Surg. Engl.* **17,** 386.
Grace, R. V., Johnson, V. S. (1937) *Ann. Surg.* **106,** 347.
Hoguet, J. P., Coley, W. B. (1918) *ibid.* **68,** 255.
Keynes, G. (1937) *Proc. R. Soc. Med.* **30,** 529.
Kocher, T. (1903) Textbook of Operative Surgery (translated by H. J. Stiles); p. 240. London.
Lytle, W. J. (1945) *Brit. J. Surg.* **32,** 441.
Marsden, A. J. (1958) *ibid.* **46,** 234.
Moloney, G. E., Gill, W. G., Barclay, R. C. (1948) *Lancet*, ii, 45.
— (1958) *ibid.* i, 273.
O'Connor, J. F. (1940) *Brit. med. J.* ii, 113.
Ogilvie, W. H. (1937) *Proc. R. Soc. Med.* **30,** 529.
Page, M. C. (1934) *Brit. med. J.* ii, 896.
Tanner, N. C. (1942) *Brit. J. Surg.* **29,** 285.

MATERNITY SERVICES IN SCOTLAND

IN parallel with the Cranbrook Committee, whose report we reviewed last week, a committee of the Scottish Health Services Council [1] has been considering maternity services in Scotland. Its report [2] concludes by saying that much of the confusion in these services seems to be related to the many choices provided and the risk of lack of continuity of medical care. Hence the committee thinks that a primary requirement is that one person should be regarded as the coordinator, and it believes that this should be the general medical practitioner. Accordingly it makes the following recommendations:

1. It should be the responsibility of the general practitioner to provide or secure the provision of all the facilities required by the mother during pregnancy, confinement, and lying-in. No problem should arise where the practitioner is himself to be responsible for the confinement, but when he is not, we regard it as essential that he should be informed by anyone else who has accepted the care of the woman.

2. A list of general-practitioner obstetricians should be introduced in Scotland. The condition of entry for practitioners not undertaking maternity medical services at the time of the introduction of the list would be an initial qualification of six months' resident experience in an obstetric unit, and the condition of retention would be a requirement to undertake refresher courses at intervals of not more than five years. Practitioners already undertaking maternity medical services at the time of the introduction of the list would be included automatically and all would be subject to removal if they did not undertake a refresher course, officially recognised as qualifying for the purpose, at intervals of not more than five years.

3. A general-practitioner obstetrician undertaking responsibility for the confinement, whether at home or in a general-practitioner bed in hospital, should visit during labour and, if possible, be present at the delivery: and the fee to be paid should have regard to this.

4. Local health authorities should instruct midwives directly or indirectly employed by them to urge women seeking to engage their services to make arrangements with their general practitioners: and the midwife should report to the local health authority in any case of difficulty.

5. Regional hospital boards should reassess, as a matter of urgency, their need for maternity hospital accommodation to provide for antenatal admissions of not less than 8 beds per 1000 births per year, together with lying-in beds for 70–75% of the total births.

6. Regional hospital boards should review the systems of admission to obstetric units, to ensure that the best use is made of the available accommodation and that the admission system in force will secure (subject to quite unforeseen emergency) that bookings are honoured.

7. The facilities of local-health-authority clinic premises and the services of their staffs should be utilised both by the hospital staffs and by general-practitioner obstetricians, who would be enabled to take advantage for their patients of all the facilities in these clinics, including those for group teaching of mothercraft or parentcraft and health education, as well as priority dental services and the provision of welfare foods (including vitamin supplements).

8. The Secretary of State should initiate action to ensure coordination by a specific requirement of a report from each regional hospital board setting out the arrangements in operation and the method of maintaining cooperation; he should have available, for consultation on the reports and on other matters affecting the organisation and content of the maternity service, a standing advisory committee under the ægis of the Scottish Health Services Council; and the reports should contain provision for the establishment of professional committees, at appropriate levels, as part of the local arrangements to ensure the smooth working of the maternity service.

1. The members were: Prof. G. L. MONTGOMERY, F.R.F.P.S. (chairman); Dr. MAY BAIRD; Dr. J. T. BALDWIN; Miss M. B. CLYNE, S.C.M.; Mrs. M. S. EWART; Miss M. FRASER, S.C.M.; Mr. C. S. GUMLEY; Dr. C. HARROWER; Prof. J. L. HENDERSON, F.R.C.P.E.; Mr. A. R. HOWIE; Mr. H. R. MACLENNAN, F.R.C.O.G.; Mr. D. MILLER, F.R.C.O.G.; Miss E. RENWICK, S.C.M.; Dr. J. RIDDELL; Sir JOHN STORRAR; Mr. A. A. TEMPLETON; Dr. N. I. WATTIE; Dr. M. E. MITCHELL (medical secretary), and Miss L. C. WATSON (lay secretary).

2. Department of Health for Scotland: Scottish Health Services Council. Maternity Services in Scotland. H.M. Stationery Office. 1959. Pp. 64. 3s. 6d.

Points of View

IN THE EYE OF THE BEHOLDER

IT was late when I finished my latest paper describing the changes we have been introducing into our hospital, and I suddenly realised how sleepy I was. On my way to bed I glanced at a newspaper [1] that was lying on the table, and my eye was held by the juxtaposition of the two pictures of St. George and the Dragon, so much alike and yet wholly different. On my way upstairs I thought, if Uccello and his colleague gave such varied accounts of so comparatively simple an incident as slaying a dragon, how would a really complex procedure like running a mental hospital strike different observers? I have often been scathing about other people's hospitals but how would mine look to them? Its merits surely would be obvious; and in bed I turned to the first page of my typescript for reassurance. But somehow it seemed to have changed. Instead of my own well-turned opening sentences I read . . .

We do not often go to other hospitals—our own patients and our duties as representatives on national and international bodies keep us too busy. But we had read so often that this hospital was good, that we looked forward with pleasure to visiting it. Everyone longs for progress, and we had a feeling of comradeship for its physician-superintendent which was in no way affected by the fact that in his articles he never seemed to describe any procedure which was not common practice elsewhere. We had also noticed that he never mentioned other psychiatrists who had used these procedures long before he introduced them. A small matter perhaps, but even if there is not time for intellectual humility it is agreeable to see a certain graciousness between colleagues. For a moment we did wonder why only one person from this hospital wrote articles; for more than one doctor must have made its progress possible.

We spent a week there. *We* could not judge a hospital on the strength of a four-hour visit. We took a tip from one of the physician-superintendent's articles; after he had shown us around each day, we made a point of going back over our route and actually spoke to a large number of nurses and some young doctors.

We have always treated our chronic patients well and have provided the same careful attention for new admissions. We were surprised to find here that the admission wards are left to the young doctors. Surely the recent and severe illnesses deserve the best treatment which can be given and this must mean the attention of the most senior and most skilled doctor? One of our informants voiced a suspicion—which we do not share—that the consultants found the careful examination of new patients too time-consuming and were loth to accept the inevitable responsibility of diagnosis. It was in fact suggested that they preferred the chronic wards because the work there was easy. Most of it was done by the nurses, and note-writing was at a minimum. Indeed we can see that it is one thing to spend many long and anxious hours in the admission wards, and another to walk rapidly through the chronic wards which have been specially emptied of patients and then to spend the rest of the day in the occupational-therapy departments or strolling through the grounds.

1. *Manchester Guardian*, Jan. 26, 1959, p. 5.

We felt that perhaps too much attention is paid to games for the patients. It seemed ridiculous to see a consultant playing with a rugger ball, and nurses lower their dignity by playing hockey with the patients. We believe that there is nothing like cricket for patients. They all enjoy watching the staff team play, and we can see no objection to them fielding or even bowling in the nets so long as the nurses do the batting. A hospital is to a great extent known by its cricket team, and patients should be encouraged to show their pride in their team by invariably watching matches in the inter-hospital league.

We paid special attention to the occupational-therapy departments, and despite the enthusiastic remarks of the nurses—we were shown round by the chief male nurse and the matron—we could discern that all was not well. For example, in one department a group of patients do carpentry in the first week, painting in the next, making lino-cuts in the third, and games' boards in the fourth. This means that no patient is ever given the chance to master anything. In fact if some patient, who has shown no interest in anything for years, suddenly discovers something that he can do and likes doing on his own, away from the noise, in a quiet corner of the room—making a mat is one actual example—we were told that he is either forbidden to do it or is moved on to some uncongenial task the following week. A patient's tastes and abilities are clearly little considered.

We were distressed by the type of film shown to the chronic patients, specially as they have no opportunity to avoid a film if they do not like it. Nature films are always good, and there are many old-fashioned comedies which would have pleased the patients and done them some good. Yet during our visit the first of a series of films on mental illness and psychological mechanisms was being shown. We saw many patients shutting their eyes, and two women—nice and intelligent middle-class housewives—said in our hearing that the film might have been about their own illness.

The physician-superintendent spoke to us with obvious enthusiasm and knowledge about classical music, and he often sits with the patients as they listen to his choice of records each week. He said that the idea was to stimulate the patients and to make them think. To us most of the patients expressed in no uncertain terms how much they disliked the counter-tenor they had just heard. The nurses, of course, did not understand the music, and we regard the business as an unfortunate attempt to impose on sick patients a culture which is alien to them.

Even in the grounds no patient is allowed to continue at one task for the whole day and has to spend half the day in the occupational-therapy department. Many patients said that they much preferred to spend the whole day gardening, but they are not allowed to settle even to this occupation (which most psychiatrists regard as beneficial). The whole policy of rapidly alternating tasks inevitably prevents the patients from enjoying one of the simplest and most fundamental pleasures of labouring man—the completion of a task he has himself started.

The nurses supervise the patients in all their activities. Nursing is an honourable and exacting profession, and in all seriousness we are bound to ask if it is the duty of a nurse to teach patients gymnastics, to play hockey with them, to dig earth and wheel barrows, to make artificial flowers?

The standard of therapeutic activity may be gauged by the fact that there is an insulin-coma unit. We heard little talk of psychotherapy and much of physical methods and drugs. For a hospital which talks so much about the social rehabilitation of patients, it was interesting to find that in one week, of the 1000 patients, 120 had electrical treatment and 249 tranquillising drugs.

Those who believe in freedom (for the patient as well as for the psychiatrist) may not like certain things we saw. We found that patients had to follow the routine of the ward. A patient might dislike changing into games clothing to do physical training, but he had to do so. If a middle-aged schizophrenic, who had washed up the breakfast things, felt like sitting in the ward and reading the paper for the rest of the morning, it was not thought that he had done his share and might benefit by being allowed free choice as to what he did for an hour or so; far from it. Out he had to go into the cold and do his exercises.

The patients were making a bowling-green. There is no harm in that, but we do suggest that the patients would have a greater sense of participation and achievement if they were permitted to complete the task they had begun. The same system of being regularly moved on to something else prevailed even here. Actually it would be quicker and more economical to have 50 patients at the job and finish it within six months, with each patient gradually learning his exact role; but apparently there are never more than 10 patients on it at once, and the green will take five years to finish. Should the other patients be denied the enjoyment or the fruits of their fellows' instructed labours?

The senior doctors and nurses pay regular visits to the kitchen and sewing-room, the laundry, and other departments. Even though these are run by patient labour, the hospital secretary could surely be trusted to see that all goes well. And is it really in the interest of the hospital to change the patients round so often? When a patient seems almost ready for discharge, she might well spend a week in one of these therapeutic departments so that she can make a small contribution to the hospital.

If the energies of the doctors are to be fully engaged and properly directed, realism is necessary. Some schizophrenics are not curable, and the same is true for the intellectual losses of old age. Is it wise and is it kind to get all these old folk out of bed? Too great emphasis is placed upon getting them back to their own homes or living with relations. There are some patients who have earned their right to stay comfortably in hospital.

Medicine and the Law

An Anæsthetist's Addiction

AT the Central Criminal Court on Feb. 20, Dr. P. W. S. Gray admitted responsibility for the death of a child to whom he had administered an anæsthetic last September. He was sentenced to 12 months' imprisonment.[1]

During the operation on Sept. 16, Dr. Gray had not switched from an empty to a full cylinder of oxygen. For three or four minutes the child's brain was deprived of oxygen, and this was a direct cause of the child's death a month later. During the operation Dr. Gray was seen to remove the connecting tube between the apparatus and the child and to put the tube into his own mouth. He was suspended from his appointment the next day.

For the prosecution it was stated that Dr. Gray, who was consultant anæsthetist at Chase Farm Hospital, Enfield, had been addicted to anæsthetic drugs for seven years, and that from the evidence of people at the hospital it seemed that this was perfectly well known. In the course of the trial one of the witnesses, Mr. W. D. Coltart, surgeon to Chase Farm Hospital, was asked by the Judge, Mr. Justice Donovan, what happened at a hospital when an anæsthetist did this sort of thing. Mr. Coltart replied:

"It is a very difficult question to generalise upon. I knew nothing about this at all. What I would have done I don't know. I think probably the same sort of thing that my colleagues did."

"May I take it that this is an unprecedented thing, or is it something to which people are prone?"—"I have heard of anæsthetists indulging in their own anæsthetic mixtures. It does happen. I have never heard of this sort of tragedy occurring. I have never before heard of an anæsthetist indulging in

1. *Times*, Feb. 21, 1959; *Manchester Guardian*, Feb. 21, 1959.

'Fluothane' . . . My own view would be that an anæsthetist would never reach a stage in which he would become incapacitated in that way. He would either become unconscious or drop to the floor. It seems to me that there must be something about fluothane which is different from other anæsthetics. It appeared to produce a state of euphoria. I think perhaps if my colleagues had realised the extra danger of fluothane they might have taken more vigorous action. Had I known of this indulgence by Dr. Gray . . . I would certainly have insisted that he gave up anæsthetics for a time and subjected himself to treatment, and if he had refused I would have reported him."

Conferences

CARDIOVASCULAR DISEASE IN EAST AFRICA

A CONFERENCE on Cardiovascular Diseases in East Africa was held at Makerere College, Kampala, Uganda, from Jan. 14 to 16 under the auspices of the East African Council for Medical Research. Prof. J. McMICHAEL (London) presided.

Range of Disorders

The background was set by Prof. A. W. WILLIAMS and Dr. A. G. SHAPER (Kampala) with a study of the range of cardiovascular disorders in Mulago Hospital. 50% of the patients were under 35 and only 23% were over 45 years of age. Contrary to some previously published impressions, rheumatic heart-disease (acute and chronic) and hypertension were common, constituting 14% and 36% respectively of cardiovascular disorders in hospital. By contrast syphilitic aortitis was diminishing (12%) and cardiac infarction rare (0·3%). Renal hypertension on a basis of pyelonephritis accounted for two-thirds of the cases of hypertension, and 80% of these patients were under 40 years old. Chronic pyelonephritis seemed to be unrelated to any detectable history of acute pyelonephritis.

Hypertension

Dr. KRIS SOMERS (Kampala) had found that the difficult therapeutic regime of mecamylamine and reserpine could be used among Africans. He showed a woman with malignant hypertension who had been taken successfully through a pregnancy on this treatment.

Dr. A. C. E. COLE (Dar-es-Salaam) agreed that most hypertension in Africans was pyelonephritic but that essential hypertension occurred among the Asians. According to Professor WILLIAMS, the upward trend of blood-pressure with age observed in European surveys did not seem to occur in Africans.

Endomyocardial Fibrosis

Dr. B. J. BALDACHIN (Bulowayo) said that, although bilharzial infestation occurred, it played little part in the production of pyelonephritis: cor pulmonale, seen with repeated heavy infestations in Egypt, seemed to be absent in Bulawayo. Endomyocardial fibrosis (E.M.F.) appeared to be described more from Uganda than elsewhere, but was commoner in natives from nearby Ruanda-Urundi than in the local population—in contrast to rheumatic heart-disease, which had the same incidence in both.

Dr. SHAPER said that the age-distribution of E.M.F. corresponded closely with that of rheumatic heart-disease, and he suggested that E.M.F. might be a modified form of rheumatic heart-disease.

Prof. J. N. P. DAVIES (Kampala) made a strong protest at the confusion of E.M.F. with other disorders, such as fibroelastosis, in many textbooks. He pointed out that E.M.F. is restricted to the lower inflow region of the ventricle, and the lesions are often sharply demarcated from the outflow tracts. Fibroelastosis by contrast is more diffuse. Loeffler's endocarditis fibroplastica with eosinophilia, in Professor Davies' opinion, is another quite separate type of endocardial disease. E.M.F. seemed to start as a thrombotic process on the endocardium.

Prof. A. W. WOODRUFF (London) called attention to the high frequency of excessive fibrosis—keloids, fibromas, &c.—in Africans. Malnutrition and possibly depressed secretion of suprarenal steroids might play some part in this.

Dr. A. D. CHARTERS read a paper for Dr. P. TURNER and Dr. P E. C. MANSON-BAHR reporting the first cases of E.M.F. from Kenya. E.M.F. was often difficult to distinguish from constrictive pericarditis; a pericardial effusion was a common feature of E.M.F.

Electrocardiography

Dr. P. TURNER (Kenya) described normal electrocardiographic patterns in the Kikuyu.

Dr. MICHAEL GELFAND and Dr. S. J. FLEISHMAN (Salisbury) presented an extensive electrocardiographic study of African labourers, police, and prisoners. Of some 600 "normals" 30 showed inverted T waves in left-sided precordial leads; the cause was doubtful.

Professor WILLIAMS and Dr. K. SOMERS (Kampala) presented material showing that E.M.F. did not produce the bundle-branch-block patterns which might have been expected in view of the scarring of the subendocardial myocardium. P-wave changes, however, were common, as in rheumatic heart-disease.

Obscure Cardiopathy

Professor DAVIES pointed out that other types of obscure cardiopathy are seen in Uganda. These included dilated hearts with endocardial thrombi and focal infiltrations of the myocardium; other cases showed patchy necrosis of the myocardium. No tropical parasites could be incriminated, but work was proceeding on the identification of a possible virus cause.

Dr. R. LEWTHWAITE (London) pointed out that the heart was often severely damaged in scrub-typhus.

Dr. GELFAND said that anæmic hearts were common, with enlargement which often receded on cure of the anæmia; the enlargement was not necessarily related to the degree of anæmia.

Ischæmic Heart-disease

Dr. R. F. A. DEAN (Kampala), using results that had been obtained in the treatment of kwashiorkor, had confirmed that animal fat (butter) produced higher levels of serum-cholesterol than vegetable fat. It seemed that differences in the amount of protein in the diet might be important in fixing the "basic" level of cholesterol, on which changes due to fat were superimposed.

Dr. SHAPER and Mr. JONES (Kampala) showed that the blood-cholesterol was significantly lower in the Africans than in the local Asian population, and the cholesterol in the African actually showed a decline over the age of 40 when the Asian was showing an increase. The Asian group, with a high incidence of coronary-artery disease and high mean cholesterol levels, used mainly unsaturated fats in their cooking. Even in African diabetes the serum-cholesterol was not significantly raised, and these patients were relatively immune to the usual vascular complications of diabetes.

Dr. CHARTERS, in an extensive study of myocardial infarction among the Asiatic population of Nairobi, had found an equal incidence irrespective of the meat-eating or vegetarian habits of the various religious groups. Animal fat might therefore be of less importance than some other factors as yet ill defined.

Professor DAVIES emphasised that coronary atheroma was not absent in Africans but was much less severe than in the Western world.

Professor MCMICHAEL referred to a paper by Lenègre [1] which showed that an alleged low incidence of coronary-artery disease in France was not due to the culinary use of olive oil but to a different habit of certification of death by French doctors. Many epidemiological studies were suspect on similar grounds, and all knew the fallacy of hospital samples and still more of "impressions". Coronary occlusion was a relatively rare incident in the vast population carrying over

1. Lenègre, J. *Rev. Practicien*, 1958, **8**, 1717.

decades atheromatous patches in their arteries. The spectrum of coronary-artery disease was enormously wide, varying from no symptoms and longevity to sudden early death. Dietary influences on blood-cholesterol levels might add slightly to the risks of occlusion, but there were many examples in which this relationship was not established. There must be other factors as yet difficult to define. Precise documentation of the morbid anatomy and comparison at all age-levels was a necessary basis for the interpretation of the very striking differences in incidence of the accident of coronary-artery occlusion.

THE LIVER

A SYMPOSIUM on The Liver, held at Ibadan University College Hospital, Nigeria, on Feb. 13–14, was organised by Prof. J. Grayson of the Ibadan department of physiology and attended by some 40 research-workers including, besides members of Ibadan University College, members of the Nigerian Medical Services, the Army Medical Services, and the Virus Research Institute of the West African Council for Medical Research.

Blood-flow

Professor GRAYSON, Dr. D. MENDEL, and Dr. T. W. G. KINNEAR (Ibadan) reported on the blood-flow in the liver of rats, guineapigs, rabbits, and monkeys. By the use of thermocouples, alterations in blood-flow could be measured as changes in thermoconductivity. Adrenaline and other agents altering the blood-pressure had little effect on the resting level of blood-flow. In that respect the liver resembled the kidney, but the regulation of blood-flow was an " intrinsic " mechanism rather than an " autoregulation ". An arteriovenous anastomotic shunt was provided by the spleen, but this was of minor importance. Splenectomy " dented " the intrinsic mechanism, but after a time this re-established itself. Though the portal vein supplied 70% of the liver's blood-flow it could be ligated without an alteration of the blood-flow. Only ligation of the hepatic artery caused a fall in blood-flow. After a time it recovered and returned to the resting level. This recovery occurred in animals when the ganglia were blocked or the nerves were sectioned, or when the spleen and suprarenals had been removed. Professor Grayson thought that these experiments showed that the hepatic artery was the primary determinant of portal inflow. The link was largely mechanical. The bigger the intrasinusoid pressure the greater was the resistance to arterial inflow. When the artery was clamped, the pressure fell from 50 mm. Hg until it reached one of 12 mm., at which stage the blood-flow was restored from the portal vein.

Fatty Changes

Prof. J. GILLMAN (Johannesburg) discussed his work on baboons, in which he had produced fatty livers resembling those seen in infants with kwashiorkor. The characteristic liver changes were rare in malnourished infants in general, and were seen regularly only in kwashiorkor. The fatty liver took 8–9 days to develop and about 20 days to dissolve. There were characteristic chromatolytic changes in the nuclei. Whereas a number of endocrine disturbances could cause fatty changes in the liver, these took 5–6 months to develop. Atrophy of the pancreas in kwashiorkor was well known. In baboons pancreatectomy caused the liver to show fatty changes of the kwashiorkor type. This effect could be partly prevented with insulin. Thus Professor Gillman could not repeat on baboons the well-known work on dogs, in which removal of the exocrine pancreatic function had been the effective procedure. In the baboon the effect of pancreatectomy could be counteracted by hypophysectomy. When such animals were then treated with cortisone mild fatty changes occurred; cortisone plus thyroxine produced more deposition of fat; but the greatest effect was obtained with the injection of human pituitary extract. No fatty changes were produced when such extracts were injected into normal baboons.

Yellow Fever

Dr. G. BEARCROFT (Yaba, Nigeria) had studied changes in the liver of monkeys infected with yellow fever. Unlike the South American and the Indian monkey, and man, the African monkey is not susceptible to yellow fever. When the African monkey is inoculated, the virus multiplies in the liver but does not cause necrosis: the monkey is therefore a true " carrier " of the disease. In the rhesus (Indian) monkey, in man, and in the South American monkey inclusion bodies are found in the nuclei of the liver cells. The processes associated with this phenomenon were studied by histochemical methods. On infection there was at first a rise in the ribonucleic-acid content of the cytoplasm. After this, the desoxyribonucleic-acid content of the nuclei increased. The desoxyribonucleic acid was at first associated with protein; later the nuclei became diffusely basophilic, the desoxyribonucleic acid also became diffuse, and the inclusion bodies were formed. These were precipitates of pure protein. The essential step in the formation of these inclusion bodies seemed to be a split between desoxyribonucleic acid and the associated protein.

Vasopressin

Dr. H. SCHNIEDEN (Ibadan) compared the effects of intravenous and intraportal vasopressin (antidiuretic hormone) in normal rats and in rats whose liver had been damaged either with carbon tetrachloride or by malnutrition. In normal rats vasopressin was inactivated by the liver; but in rats with damaged livers its action was the same whether it was injected intravenously or through the portal vein.

Malaria

Prof. B. G. MAEGRAITH (Liverpool) discussed the disease process of malaria in liver. The liver was always affected in malaria. An acutely damaged liver was swollen and blue; its edges were rounded, and the blood-flow in the hepatic veins was greatly reduced. After the clamping-down of venous outflow the arterial and portal inflow became reduced. Hence the centrilobular portion was most easily damaged. There was a double circulation—the arteriovenous anastomoses running like a sleeve at the edge of the portal tract were an alternative to the sinusoidal circulation. Malaria parasites caused an overall reduction of oxidative processes. There was no change in the hæmoglobin molecule, but the glutamic-acid oxidase was reduced in activity. It could be reactivated in vitro by the addition of coenzyme I. There were thus two stages in the liver damage in malaria. At first came the circulatory effect, which was probably a nervous response. Sympathectomised rhesus monkeys show no central lobular damage. This stage was reversible. The second stage, which caused the irreversible damage, affected the respiratory processes regulated by the mitochondria.

Liver-function Tests

Dr. J. C. EDOZIEN (Ibadan) discussed the results of liver-function tests in surveys at Ibadan. The plasma of the local population was often very yellow. The pigment, which could also be found in the subcutaneous fat, was not bilirubin. More of it was found in normal plasma than in plasma from malnourished children. It was not yet certain whether it represented the colouring matter in palm oil. Sulphobromophthalein sodium injected at 5 mg. per kg. body-weight was excreted to more than 95% within one hour if the liver was normal. The cholesterol level was lower in Ibadan Africans than in the local Europeans. Within the African population the cholesterol level was higher in the higher-income groups. Regardless of what the absolute level amounted to, the ratio of free to esterified cholesterol was 1 to 2 provided the liver was healthy. Electrophoresis of the serum-protein with subsequent staining for lipoproteins showed an absence of the α-lipoprotein fraction in liver disease. The cholinesterase level was the same in healthy Africans and Europeans. The same applied to other enzymes—the serum amylase, isocitric dehydrogenase, and glutamic-oxalacetic and glutamic-pyruvic transaminases. There was a high β-amino-oxybutyric-acid excretion in kwashiorkor. In the aminoacid chromatogram, sera from patients with liver disease showed a deficiency in methionine, cystine, and phenylalanine—aminoacids which were found more in albumin than

in globulin. Was the high gamma-globulin seen in Nigerians caused by a dietary lack in these aminoacids, or was it due to an increase in immune antibodies which were found in the gamma-globulin fraction?

Cirrhosis

Prof. G. M. EDINGTON (Ibadan) discussed the incidence of cirrhosis of the liver in West Africa. In a village survey in Ghana he had found liver enlargement in 18·5% of apparently healthy schoolchildren and in 33% of healthy adults. Liver and spleen enlargements were associated. There was no difference in sex-incidence in the children, but in the adult liver enlargement was twice as common in women. Both malaria and malnutrition seemed to be agents in causing enlargement of the liver. In postmortem material cirrhosis was seen more in men than in women, and hepatitis was commoner in women than in men. Kwashiorkor, on the other hand, was found equally in children of both sexes. In 600 consecutive postmortems in Ghana portal cirrhosis was not seen to be connected with any one specific condition. Certainly protein malnutrition was not the only cause of cirrhosis. Siderosis of the liver was frequent in Ghana but infrequent in Nigeria.

Pseudocholinesterase

Dr. H. LEHMANN (London) discussed the role of pseudocholinesterase in liver disease. The serum-pseudocholinesterase level was fairly constant in individuals, though there was a wide normal variation. A rise or fall of the enzyme level in any one patient, even if it occurred within the " normal range ", was useful as a guide to changes in liver function. The wide normal range was due to the presence of two genes determining the pseudocholinesterase level, one causing a high and the other a low enzyme concentration. Homozygotes for the first gene did not have a better liver function than heterozygotes, though the pseudocholinesterase level was lower in these heterozygotes. Fortunately, in Europeans at least, homozygotes for the low pseudocholinesterase gene were rare. Thus the overall value of the measurement of pseudocholinesterase as a test for liver function remained.

Peritoneoscopy

Prof. W. W. DAVEY (Ibadan) described the results of peritoneoscopy in liver disease. The procedure was simple and could be carried out with one incision under local anæsthesia. Liver biopsies could be obtained from areas most likely to be anatomically altered.

Public Health

Influenza

INFLUENZA continues to be prevalent in many parts of Britain, including Glasgow and Edinburgh, the North-West and Midlands of England, and the London area. In the week ended Feb. 14 deaths from influenza in England and Wales totalled 455, compared with 144 in the week ended Feb. 7 and 54 in the week ended Jan. 31. Of the 455 deaths, 377 were in patients aged 55 or over. In some outbreaks virus A (Asian) has been isolated, and in others virus B.

In the London area the influenza epidemic started to affect the number of applications to the Emergency Bed Service on Jan. 29. The weekly total of applications up to midnight on Jan. 28 was 1490. By Feb. 2 the applications had risen to 1720; and, since many hospitals were experiencing difficulty in admitting all applicants, a red warning was issued. This warning was immediately effective in making more beds available for urgent admissions, and in consequence many doctors were able to admit direct and the application-rate fell to 1660 by Feb. 7. Thereafter, however, the hospitals began to have ever-increasing difficulty in admitting patients, and by last Tuesday (Feb. 24) the applications had reached 2420, which is only 120 below the peak of the great fog of December, 1952. On that occasion the pressure only lasted a few days, whereas now it has been going for four weeks.

In England Now

A Running Commentary by Peripatetic Correspondents

A SPECIAL congress of the Camerian Research Federation to commemorate the fourth anniversary of the discovery of yenwupongine [1 2] was held on board the s.s *Aurora* and in Honolulu last month.

Among the many important papers read out loud was an outstanding contribution by ABE QUABE,* SAM FINKELHOOFER IV,† and HYRAM D. SMITH, Jr.,‡ describing their new bioassay of H.N.Y.W.P. in the lacrimal fluid. Secretion, stimulated by a variety of ingenious techniques, was quantitated in a metrically calibrated transoptic circumferential container†. Fractionated aliquots of the fluid, purified by papyraceous tissue filtration, were then eluted with unconjugated hydrosulfated pseudo-chondroitin SO_4–B at pH 4·17, and the final solution injected into 8-week turkey embryos. Interference with a number of metabolic pathways resulted in a variety of developmental aberrations, including gonadal dysgenesis, as shown by abnormal comb growth in cocks and egg production in hens. The concentration of H.N.Y.W.P. in the lacrimal fluid could then conveniently be calculated from the formula:

$$C = 9{\cdot}7438 + \frac{pK \times \Delta\ Tsp\ (\log H.N. - \text{semilog } Y.W.P.)}{\sqrt{\text{eggs/week}}}$$

In the ensuing discussion, Dr. ELMER KNUT congratulated the authors on a swell piece of work. Dr. IRVING KATZ expressed his delight that we were beginning to talk turkey in a difficult field. Dr. ED LI YI, criticising egg counts, urged that one must look some place else for the perfect endpoint. Dr. JAY JEROME thought we should be much wiser if we knew what was going on in the doggone ovaries. He suspected that all the follicles had gotten shot to heck. Dr. IRVING KATZ guessed so too.

In reply, Dr. QUABE thanked the speakers for their interesting comments. Concerning the metabolism of H.N.Y.W.P. there was a good deal of monkey business we still had to get to the bottom of, and further work was proceeding with this in mind.

* * *

When I showed last week's Socratic dialogue (*Lancet*, Feb. 21, p. 407) to my friend Cynicus he read it with interest, but he said that his own definition of a committee was " a group of people who individually can do nothing and who collectively agree that nothing can be done ".

* * *

Taking an old and treasured car to one of those dazzling, efficient garage places is very like taking your youngest and tenderest offspring to the dentist. I was left sitting in a waiting-room lined with rows of books and journals on the diagnosis and treatment of automobilic disorders, and the communicating door to the surgery was gently but firmly closed. Unnerved by the grim backs of the bound journals, I went out into the showroom where, after standing forlornly between the ranks of shiny, sneering, new cars for a few minutes I decided that the waiting-room was better after all and nearer to my poor little patient. But when prolonged hissing noises began to issue from the surgery I had an attack of tachycardia and wished that I had never come at all. A series of crescendo whines told me that the very vitals of my faithful were being strained to their utmost, and cruel grinding sounds set me pacing agitatedly up and down the bright contemporary carpet, refraining with difficulty from biting my nails. An attendant erupted into the waiting-room once or twice, but paid no attention to my anguished look of inquiry,

1. *Lancet*, 1955, i, 917
2. *ibid*, 1956, i, 747

* Associate Professor of Clinical Yenwupongology, Medical Service and 1st Medical Division, Department of Medicine, Yenwupongine Station and Research Laboratories, The Hiawatha Clinic and Hospital, Hiawatha Medical Center, University of Hiawatha, Hiawatha, Hi.

† On a grant from Glass Bottles Inc.

‡ Formerly technician, British Egg Marketing Board.

and I could not trust myself to speak. After what seemed an eternity someone came out to describe the trouble and ask me to return in a couple of hours. I went dejectedly out, feeling like a traitor, sick at heart, and full of doubts and fears (I had just glimpsed through the half-open door one of the mechanics delivering a smart kick to the flank).

When I did return all seemed to be well, though I detected an aura of reproach about the patient; but she took me home briskly, faithful as always, loyal to the last, and none the worse for her ordeal.

* * *

It is usually the younger members of the family who insist that their parents must live with the times. The ordinary radio and gramophone are not good enough, and we are asked to consider " hi-fi " and multi-speaker equipment. But by very good fortune I find that I have suddenly become stereophonic and can enjoy the delights of this type of sound without recourse to expensive and up-to-date apparatus. The miracle took place about a week after my stapes mobilisation while I was listening to Rimsky Korsakoff. The tympany and lower notes came over on the operated side, whereas the flutes and short strings were clearly heard by the opposite ear. Subsequent audiograms show an improvement of some 30 decibels for most of the lower frequencies as a result of the operation, while the other ear has maintained better conductivity for the higher frequencies. My young son suggests that he would like one of his ears adjusted to give a " tweeter " effect. I am indeed grateful to my E.N.T. surgeon.

* * *

New York and London taxi-drivers are renowned for their pithy and sometimes profane remarks. No doubt Montreal has its quota of wits and blasphemers (in both languages), but it has its poets, too. Last night my secretary was talking to her driver, and in the course of conversation he told her that his wife and he had recently lost twin baby girls, three or four days after they were prematurely born at 7 months. " You see," he said, " the whole trouble was they were so small they forgot themselves."

* * *

In the Garden—III.

WHAT'S YOUR GNOME? MINE'S ONLY A COGNOMON

When Adam was delving he found a stone
And showed it to Eve as she span.
"It's rather twee, it looks like me,"
And that's how it all began.

Eve painted its nose and lacquered its toes
And put it out on the grass,
And a passing motorist pulled up short
And said "Why that's first-class!

"I bought Lot's wife, after trouble and strife
But she melted and looked forlorn.
You'll see tomorrer a Brighter Gomorrah!"—
And garden elves were born.

Much later the Jews sold them off to long queues,
As they wept under *S. babylonica:*
King Neb. filled his Rolls—or so say the Scrolls—
At least it was some very toney car.

Next appeared leprechauns and rabbits and fawns
Under toadstools and other Godwottery,
And fairies and pixies got up to their trickses
In stone (artificial) and pottery.

All this makes me queasy; but carping is easy
And p'raps there's a lesson to teach.
I suggest, as placebos, Greek urns and gazebos
Are not within everyone's reach.

So remember, in Ilford, and even in Guildford,
Plaster dwarfs in a Walt Disney garb'll
Supply the same measure of æsthetic pleasure
As the Venus de Milo in marble.

ENVOI

Miss Jekyll's Boots, in concrete, will adorn
The mossy sweep of my two feet of lawn.

Letters to the Editor

THE CRANBROOK REPORT

SIR,—The Cranbrook Report has been published, and with it we have read last week your excellent leader and the most interesting article by Mr. T. B. FitzGerald. That the report leaves the maternity services still divided we read with dismay, if not with despair. These services are divided in control, divided in responsibility, and divided even in outlook. Of this we are made very much aware in our work in three large hospitals. We are never allowed to forget the disadvantages, to patients, of a lack of coordination.

What a chance has been missed; for, even if the committee had advocated wholeheartedly a unified service, to institute this would have taken so long a time as to transform its development into a process of evolution. A unified maternity service is bound to come, but the clock has been set back at least ten to fifteen years. And this has happened in spite of two reports from the Royal College of Obstetricians and Gynæcologists in 1946 and 1956, which gave identical advice as to the necessity of such a service.

Apart from the expression of a wish for close cooperation between those who look after the woman in her pregnancy and confinement—a wish that has been often expressed before—we find no constructive proposal in the report. It adds to our sorrow that the report (supported by your leading article) advocates the formation of yet another group of semi-administrative " local maternity liaison committees ". We live in an age of committees ad nauseam. They involve endless waste of time and an enormous amount of office work. When they reach a decision it is usually out of date and often unpractical, and—worst of all—nobody accepts any responsibility. To establish yet another set of committees would be of little or no use. For some years we have all had experience of trying, sincerely and conscientiously, to link up (by letter, telephone, or personal attendance) the various individual parts of the service, and we know that too often this turns out to be wasted effort.

The Cranbrook Committee must have had some doubts on the wisdom of discarding all thought of a unified maternity service, for they say that if information were forthcoming from a pilot scheme it would be welcome. Such information was in fact given them in Mr. FitzGerald's paper when this was presented to them in a personal memorandum. Evidence of a coordinate scheme could be found in the records of the work done in Aberdeen under the direction of Prof. Dugald Baird; and in England for some years a serious, and successful, attempt has been made at Oxford to integrate into one working service all those interested in and responsible for maternity.

Mr. FitzGerald is, we believe, correct when he suggests that many mothers could return home, not only in safety but with advantage, 48 hours after delivery. It is probably true that the great majority of women would like to be certain that their *confinement* could take place in a hospital, but of these a very large proportion, we know, would be glad if they could spend the " lying-in " period, or puerperium, at home—especially if during these two weeks or so they could be assured of regular visits from their midwife and occasional visits from their doctor. That many women prefer to be in their own homes during the lying-in period is, of course, not an argument

in favour of home *confinement*. It is the failure to appreciate this fact that has befogged all discussion of the relative merits of a hospital or domiciliary service.

In the absence of an extensive, expensive, and possibly unnecessary building programme, the present shortage of obstetric beds in certain regions cannot be overcome, except by the policy of a shorter stay in hospital after the confinement. Such a policy, when previously suggested, has been cast aside as too troublesome in that it would interfere with what may be termed " vested interests ".

A last point we wish to make is that the shortage of midwives may well be directly due to the fact that members of this branch of the profession feel dissatisfaction and frustration at the continued absence of an effective maternity service. Until such a service is achieved, we must all of us expect to flounder slowly and laboriously towards our ultimate goal.

A. JOSEPH WRIGLEY
GORDON W. GARLAND.

St. Thomas's Hospital, S.E.1.

OBSTETRICS AS A DISCIPLINE

SIR,—I enjoyed Prof. Andrew Claye's humorous and searching essay (Feb. 7) in which he sides with Dr. Slop against the " ignorant old woman ", the midwife. Fortunately, both Dr. Slop and his rival the handywoman are now history, and surely the time has come to regard any competition between the modern general-practitioner/obstetrician and his skilled counterpart, the midwife, as history.

The midwife should, I believe, be encouraged to unite forces with her colleagues in medical practice continuing as at present to take a vital part in the antenatal care and, of course, attend her patient during labour. Many practices in the Midlands have already achieved this type of splendid work, both members of the team meeting for regular antenatal clinics.

Professor Claye advises colleagues in practice to dispel fear from their patients by saying " When you are having your baby I shall be there ", and I agree that even a busy practitioner can make it his business to visit during labour; but to attend all deliveries is quite another matter. If he is absent attending to some other ill patient, he is only too glad to know that his obstetric patient is safely in the hands of his trusted midwife. She is perfectly capable of dealing with normal labour, and her training and experience allow her to recognise abnormalities if they arise and therefore to send urgently for help from her colleagues in practice or directly to hospital (e.g., the flying-squad for postpartum hæmorrhage). In other words, as long as there is domiciliary midwifery the patient must have the services of a skilled midwife.

I am a little perturbed at the implication to be drawn from Professor Claye's parallel between the doctor and the conductor of an orchestra. Surely if he conducts there is no need for the conductor to play all the instruments!

In hospital practice the obstetric team includes expert and experienced labour-ward sisters none of whom really look forward to the days forecast by Professor Claye when they may have to call the doctor for normal deliveries. They do at present call the students and new house-surgeons but usually as part of their responsibility as teachers. I am also worried at the possible effect on recruiting the right type of pupil if it becomes known that senior obstetricians are advocating that the midwife should always play a spectator role at delivery, for she looks forward keenly to her senior days when as a midwife she will have responsibility for " her " mothers and " her " babies—a point brought out by Mr. Frank Stabler in the same issue of *The Lancet* (p. 299).

In a teaching unit where student and pupil midwife work and learn together in the wards and labour wards, there is great emphasis on teamwork. To remove from our midwives the conduct of labour would break the team spirit and, in fact, reduce the midwife's status to that of obstetric nurse. Moreover, I believe the post of obstetric nurse would attract very few recruits of the type we need in obstetric departments; and, of course, she would never be competent to take full responsibility in domiciliary practice.

Should we not end up with tiered bunks on the American style for the sleeping-in obstetrician in the labour ward? There he would not be called by a skilled and reliable midwife but by a nurse or obstetric nurse to record the fœtal heart, to make a vaginal examination before sedation, or perhaps to pass a catheter. Nor would the doctor's sleep alone be at stake; for I believe that in the long run his patients would suffer a great loss by the disappearance of the skilled and devoted midwife.

I do hope Professor Claye will consider the problem again before he advocates the replacement of the midwife at delivery by the doctor.

> Truce! truce! good Dr. Slop,
> Stay thy obstetrick hand,
> Return it to thy bosom
> . . . to keep it warm.[1]

Queen Elizabeth Hospital,
Birmingham, 15. H. C. MCLAREN.

ADMINISTRATION OF HOSPITALS

SIR,—Mr. Way (Jan. 10) and Dr. Avery Jones (Jan. 24, Feb. 21) have done a great service in drawing attention to the grimy state of hospital walls, but that this has been tolerated for years is surely symptomatic of the malaise affecting the administrative structure in the hospital service. No doubt men of the calibre of those who ran the hospitals before the war (with a fraction of present-day staffing) still exist, but they must be set free. Never was there a greater need for decentralisation and a return to honest-to-God management by those on the spot instead of remote control, ponderous, and enervating in its denial of responsibility.

And now, Sir, there is talk of a need for more guidance from the centre. If this means advisory and research departments set up by the Ministry, well and good; but it surely means more control and obstruction. Has power corrupted so thoroughly that those at the centre cannot see the futility of such a course; are not the lessons of the past ten years as apparent to them as to most doctors working in the service? Is the profession forever willing to tolerate the situation where the Government of the day listens over much to the voices of those who have too often achieved eminence by virtue of political or administrative dexterity?

Now we read of likenesses being drawn between Services, armed and otherwise, and the hospitals. It is encouraging that *The Lancet* has perceived the danger of such thinking. For any similarity is superficial because of the complex skills and human problems with which the hospitals must contend: it is ludicrous to think of them in the same context as brigades, divisions, factories, or broadcasting stations.

I respectfully suggest the following reforms, or something like them. The proposal of a system of block grants made (and forgotten?) by nearly all the witnesses before the Select Committee on Estimates (1950–51) should be acted upon; Treasury opposition may be expected. The administrative unit should be the hospital management committee, with suitable adjustment for those at present too big or too small. Block grants for three or five years should be made to H.M.C.S directly. Regional hospital boards should be abolished, for they are attempting the

1. Laurence Sterne. Tristram Shandy (1760).

impossible. Vital decisions are too often taken there by people barely acquainted with the areas affected; plans float from office to office for years, and one has only to sit in an R.H.B. office and listen to a few telephone conversations to know the nonsensical petty detail with which they struggle over hundreds of miles of country. It is a compliment to the energy of their staffs that they achieve what they do, but it is quite, quite wrong. Some of their abler servants will be needed to put new blood into the Ministry, and the rest to strengthen the H.M.C.S.

There is much to be said for a director-general at the Ministry of Health; he would naturally have power of appointment to H.M.C.S, and of inquiry into the affairs of areas suspected of backsliding and inefficiency.

The pristine status and salary of the key position of hospital secretary to the larger hospitals should be restored; it should hardly be less than the group secretary and one would like to see him directly responsible to the H.M.C. itself. By doing these things the H.M.C.S should attract again those able laymen who of old gave lavishly of their time and experience, and so many of whom long ago resigned their seats on the H.M.C.S through utter frustration, knowing that almost all their efforts could, and would, be brought to naught by some person or persons at a distance, inevitably ignorant, sometimes uninterested, and occasionally antagonistic to local needs.

Above all, forms and returns must be reduced to an essential minimum, there should be fewer committees, and more management by a smaller, higher-paid, competent executive.

Perhaps those teaching hospitals which have known gentle interference and procrastination at Ministry level will spare the R.H.B. hospitals a shred of sympathy in their plight, and remember them when reform of the Health Service is eventually considered.

Ipswich. J. W. PAULLEY.

TRACHEAL FENESTRATION

SIR,—Referring to your annotation on this subject (Jan. 10), we wish to call your attention to our publication on the same subject [1] which preceded those quoted by you.

We described the crucial clinical observations, first made by us, on the effect of continued daily suction in the depth of the airways through a tracheal opening with catheters passed by the patients themselves. This treatment of pulmonary cripples had been practised by us in a few cases over nearly a decade. Favourable experience so gained first led us to tracheal-fenestration experiments in animals. So it was upon our initiative and with our collaboration that Dr. Rockey elaborated his procedure for tracheal fenestration. The results of this experimental work were published in an article by the three of us.[2]

Since tracheal fenestration is our brain-child we were naturally reluctant to criticise it, but clinical experience in cases operated upon by Dr. Rockey soon forced us to a sobering verdict. To quote Voltaire, we realised that "It contains much that is new and good, but alas, what is good is not new and what is new is not good". In a second article [3] we voiced our disapproval of the Rockey procedure requiring two openings into the trachea, objectionable for more reasons than we have space to relate here. As you pointed out in your annotation, surprising results were obtained in patients without secretions or cough. Indeed the most striking results were obtained in just such cases. For this and other reasons mentioned in part in both our articles we have concluded that excessive secretions are not a proper indication for tracheal fenestration. We felt the need to issue a warning against misuse of tracheal fenestration as a short-cut treatment for profuse cough and expectoration, lest some day patients may have their "throat slit" for simple bronchitis.

At the present time several surgeons are performing permanent tracheostomies by simple procedures with single tracheal openings which afford the advantages of continued suction without resort to the formidable operation of Dr. Rockey which requires two tracheal openings. We were indeed glad to note from your excellent editorial on "Tracheotomy Today" in the very next issue of *The Lancet* (Jan. 17) that your surgeons and physicians have made use of this therapeutic method in pulmonary cripples and are fully aware of its potentialities for both good and evil.

New York. EDGAR MAYER.

1. Mayer, E., Blazsik, C. F., Rappaport, I. *J. Amer. med. Ass.* 1958, **167**, 696.
2. Rockey, E. E., Mayer, E., Rappaport, I. *Dis. Chest*, 1956, **30**, 224.
3. Mayer, E., Rappaport, I., Blazsik, C. F. *J. Amer. med. Ass.* 1958, **168**, 169.

TESTOSTERONE IN DEFECTIVE SPERMATOGENESIS

SIR,—In reply to Dr. Bernard Sandler's question in his interesting letter (Feb. 14), we write to state that in the case of the azoospermic patient whose wife became pregnant, examinations for spermatozoa in a postcoital specimen of his urine and in the wife's postcoital test were not performed.

St. Bartholomew's Hospital, London, E.C.1. A. W. SPENCE
V. C. MEDVEI.

PAPER ELECTROPHORESIS IN DIAGNOSIS OF LUNG CANCER

SIR,—Verleur and Stolk [1] demonstrated that certain changes of protein spectrum occurred in mice with a transplanted mammary carcinoma (Odz-strain, Antoni van Leeuwenhoekhuis, Amsterdam). When mice were treated with methylandrostenediol the changes in the serum-protein seemed to be inhibited. They used the paper-electrophoretic method described by Oosterhuis.[2]

Verleur [3] recently standardised this, and established with certainty some deviations of the serum-protein spectrum and curve (electropherogram) in patients with pulmonary carcinoma. He assumed six criteria for the diagnosis of carcinoma: a decreased albumin content, an α_1-globulin peak separated from the albumin peak, a rise in the α_2-globulin peak, a rise in the α_2-globulin peak as high as the β_1-globulin peak, a small and sharp α_2-globulin peak, and the separation of the α_2-globulin peak by a deep recession from the β_1-globulin peak.

In this way the sputum of patients with pulmonary cancer was examined by Verleur et al.,[4] but, unlike Warfvinge,[5] they could find no distinction between the analysis in cancer and in chronic bronchitis. So this investigation was not pursued.

An extensive study was made of the serum analysis in pulmonary cancer. In 94 out of 149 cases (63·1%) the result was positive. False-positive results were obtained in only 5% of cases, when the analysis could be continued during the course of the disease.

The examination was positive in early cases (coin lesions) in 62%. A distinct relation between the radiological findings in pulmonary carcinoma and the paper-electrophoretic protein spectrum could not be established; neither was there any relationship with the anatomical type of cancer.

1. Verleur, H., Stolk, A. *Proc. Acad. Sci. Amst.* 1956, **C 59**, 587.
2. Oosterhuis, H. K. *J. Lab. clin. Med.* 1954, **44**, 280.
3. Verleur, H. Thesis, Free University, Amsterdam, 1958.
4. Verleur, H., Gerrits, J. C., Stolk, A. *Acta physiol. pha* [illegible] *.néerl.* 1956, **5**, 220.
5. Warfvinge, L. E. *Acta med. scand.* 1955, **153**, 49.

In patients with pulmonary carcinoma and metastases the albumin content was significantly lower and the α_2-, β_2-, and γ-globulin values deviated more.

The standardised method of paper electrophoresis of the serum seems to be an important means of establishing the diagnosis of pulmonary carcinoma, especially when the analysis can be continued at monthly intervals during the course of the disease.

J. C. GERRITS
A. STOLK
H. VERLEUR.

Histological and Chemophysiological Laboratories of the Free University, Amsterdam.

MENTAL HEALTH BILL

SIR,—Regrettably, Dr. Bickford is in error in suggesting that the Bill envisages the removal of the medical superintendent from the mental hospital. Desirable as this would be, something much more limited is in fact intended. Responsibility for none of the functions he mentions—food, clothing, heating, lighting, furniture, &c.—is in any way affected by the Bill, which does not deal with matters of this kind; though why he imagines that the chairman of the medical advisory committee, speaking for the medical staff as a whole, should not have infinitely more authority than the medical superintendent, speaking for no-one but himself, is beyond comprehension.

It is no longer possible to disguise the fact that staff relations in many mental hospitals are virtually at the point of breakdown. The exceptional hospitals where this is not the case are all administered by quite exceptional people who have a flair for making the near-impossible work. Unfortunately, most people are not exceptional; and an administrative system which requires the exceptional is demonstrably unsatisfactory.

Now that mental hospitals are staffed by clinically independent teams headed by consultants of equivalent status, instead of the former hierarchy of assistant medical officers dominated by an authoritarian superintendent, the administrative system of medical superintendence is just as catastrophic in its effects as it is agreed to be in general hospitals. The situation is, however, made infinitely worse by the existence of various legal instruments which further bedevil relations between medical superintendents and consultant staff; and it is difficulties which arise from the operation of these which the Bill will resolve.

Let us consider the kinds of thing which happen at present:

Admission and discharge, parole, leave, and various special reports are at present legally the responsibility of medical superintendents. They are normally delegated to consultants because any other arrangement would be hopelessly complicated, but at the same time powers of haphazard intervention are retained and used quite arbitrarily.

A patient's discharge from hospital is used as an opportunity for interference, which should not, I suggest, be judged by the frequency with which a consultant's recommendations are altered or reversed but by the frequency with which the incident of discharge is made the occasion for intervention in a clinical relationship. In many hospitals it is the practice for the medical superintendent to have a discharge interview, usually with a patient whom he is now seeing for the first time. This is futile and an utter waste of time; but the main objection to it is that it interferes in a clinical relationship.

In the case of certified patients who are to appear before a discharge committee, this interview is of course justified by reference to the medical superintendent's legal responsibility for making recommendations for discharge under section 77 of the Act. But it is quite ludicrous that these patients should be presented to the committee not by the consultant who has been clinically responsible for weeks or months but by someone else, usually on the strength of one brief interview; and it is even more ludicrous that on this slender acquaintanceship a consultant's recommendation may be altered. Under these conditions I have known it to happen that the account given to the committee members concerned not the patient being interviewed but another still waiting in the queue outside, because he was not recognised after only one previous brief interview. This is to make an utter mockery of the whole proceedings; and, though one can circumvent this pantomime by arranging for the discharge of patients under section 72 of the Act, when they will have usually departed before any such interview can be arranged, this is unsatisfactory because it tends to give relatives a wrong impression and to falsify statistics as well as precluding the arrangement of periods of "trial".

In many hospitals voluntary patients are also paraded for a discharge interview, and protests are countered by the assertion that discharge is a medical superintendent's responsibility. In consequence I know of patients of a dependent and inadequate type who, after much effort and encouragement, have reached a point where they have given notice to leave only to be persuaded to withdraw it at this interview. Yet the consultant in clinical charge is expected cheerfully to pick up the threads and deal with the impossible clinical situation which now arises.

In some hospitals, patients who by no means can be regarded as emergencies arrive for admission, arrangements having been made by the medical superintendent without any reference to the consultant whose beds are to be occupied, and protests are answered by reference to his responsibilities under the Acts, though in my own hospital this particular difficulty has largely been eliminated after the adoption of a scheme emanating from the medical advisory committee. Parole and leave are normally granted by the clinically responsible consultant or by a junior on his behalf; but alterations can be made by the medical superintendent, perhaps after discussion with the nursing heads, without the consultant in clinical charge being informed and even without the patient being seen.

The completion of special reports of various kinds creates numerous difficulties.

Special reports to the Board of Control and recertification constitute little difficulty, because few medical superintendents could undertake the work involved in writing these—though it is worth noting that, simply because it happens to be convenient, no legal difficulty is met with in delegating this responsibility to other members of staff by using the polite fiction of signing as "Acting Medical Superintendent". Other special depositions and affidavits are much more jealously guarded superintendents' functions, though just how unsatisfactory it is that these should be completed largely on hearsay and by someone without first-hand knowledge rather than constituting the "best evidence" available is now being recognised by the courts (see comments of Lord Merriman in the case of Usher *v.* Usher).

Even death certificates cause difficulty. For voluntary patients the Mental Treatment Rules, 1948, are specific in that the responsibility lies on the registered medical practitioner attending the patient during his last illness. Nevertheless I have had to demand this right, which is still not satisfactorily conceded. For temporary and certified patients, though the medical superintendent is responsible for sending the notice of death and statement to the Board of Control, it is not made clear who is responsible for its preparation and signature, though any arrangement which permits its completion on hearsay must be demonstrably unsatisfactory. I have had much trouble on this account, the issue coming to a head because, after the death of a voluntary patient under my care whilst undergoing treatment, I informed the coroner direct, sending a written statement of circumstances, a copy of which was submitted to the medical superintendent for his information. Though he had at no time seen this patient, I was informed that

this procedure was "deplorable", because contact with the coroner was a medical superintendent's function—a thesis I was not and am not prepared to accept, since the only information he was in a position to supply was hearsay. Despite this I was neither notified of the time and place of the inquest nor requested to attend, and only subsequently did I learn that it had been convened and that he had attended and given evidence. I still have no information about the proceedings though they could easily have involved me in a most direct fashion.

In some hospitals, from the argument that the medical superintendent is responsible for admission, leave, and discharge, it is asserted that such matters are involved in almost every letter that is written by a consultant—not least important those which are sent to general practitioners on a patient's discharge.

I have known of instances where consultants have been refused the right to sign letters on their own behalf, and some time ago I discovered that my own letters, after signature, were being taken to the medical superintendent's secretary, who perused them and referred such parts as she saw fit to question to the medical superintendent—a state of affairs which came to light when I was asked to make certain alterations. Vigorous protest resulted in the impropriety of this being conceded.

If now to all this is added the fact that any patient can not only arbitrarily be moved out of the care of one consultant to that of another (something which admittedly happens only rarely) but also be summoned to an interview with the medical superintendent at any time and without the doctor responsible being either informed or consulted (something which happens continually), a picture builds up in which the "autonomy" of consultants in clinical matters is nothing but a polite fiction.

Trivial as each of the issues which I have described may seem, together they create a situation in which it is quite impossible for a consultant to maintain a proper relationship with his patients. Here of course one comes to the central issue. Whose patients are they? A letter from the Ministry of Health to the Sheffield Regional Hospital Board dated March 17, 1950, which is supposed to deal with this issue of medical-superintendent/consultant relations is most revealing. Though it speaks of the "complete clinical freedom" of the consultant, in the last paragraph we find: "Wise administration would no doubt secure that the Medical Superintendent would be able to maintain close contact with all *his* patients." Ridiculous as this suggestion may be in a patient population of 2000, they are still "*his* patients". When it becomes patently obvious to patients that vital issues such as parole, leave, discharge, inquiries from their relatives, and whether they are to be divorced or no, are decided not by their own consultant, but by someone else "in charge" of him, his status, and therefore their confidence, must inevitably be debased. Psychiatry above all specialties requires a proper rapport between doctor and patient, and it is especially invidious that this relationship should be impaired in a way that no self-respecting physician or surgeon would tolerate.

If the Mental Health Bill becomes law in its present form, responsibility for all these matters will be vested in the "responsible medical officer" defined as "the medical practitioner in charge of the treatment of the patient". Though I have heard sneering references to "the irresponsible medical officer" by those who presumably wish to conjure up a picture of patients being detained on the authority of some junior and newly qualified house physician, such a definition can refer only to the clinical consultant ultimately responsible for the treatment of the particular case. It would be difficult indeed to produce even the semblance of a convincing argument against a much overdue reform of this kind; and this I suppose is why Dr. Bickford seeks to misrepresent what is proposed as involving the continuance of medical superintendency as a system—which of course allows him to raise again the old bogy of the lay administrator to scare the timid. He need have no fear that for the present he will be unable to choose his hospital's furniture; but I cannot help suspecting that what disturbs the medical superintendents more is the proposed abolition of those indefensible statutory responsibilities with which they bolster their authoritarian rule.

CONSULTANT PSYCHIATRIST.

SIR,—As we are psychiatrists, let us call a spade a spade. The fact is that our brother consultants are banding together to (symbolically) murder the horde-father, the medical superintendent. But history has a habit of showing that sooner or later a new leader is installed. This is adumbrated by Dr. Frost's letter last week in which we are told that the chairman of the medical advisory committee should have "authority" and should be "untrammelled". For practical purposes such a person will act as a medical superintendent in everything but name. The debate reduces itself therefore to whether the medical superintendent should be appointed by the management committee and regional hospital board or by election from the medical staff. We must not assume that the doctor who is the cleverest in obtaining votes from his colleagues is necessarily the most competent administrator.

ANALYST.

SIR,—Several of your correspondents have written of the necessity for changes in the administrative arrangements in mental hospitals. I have been surprised that the official organisations—notably the Royal Medico-Psychological Association and the British Medical Association—have not taken the opportunity of giving a useful lead to the Government about this matter. The Board of Control has added greatly to its laurels by planning much of this excellent Bill, and it is rather unfortunate that the medical bodies concerned have not seen fit to follow this example.

There is no doubt that much of the responsibility for administration in mental hospitals should be entrusted to medical staff committees as is the practice in general hospitals.

Many will argue that this will mean a greater transfer of power to the hospital secretary. There is no reason why this should be so, and it is difficult to visualise a hospital secretary who would fail to accept the reasonable opinions of a group of well-informed and united consultants. Furthermore, medical committees can easily enhance their status with management committees by making certain that their recommendations are based on sound practical knowledge and that the advantage to the hospital of these proposals is recognised easily.

It may be argued also that hospitals in remote areas do not have sufficient staff to organise a good medical committee. Apart from the consideration that such hospitals are obviously understaffed and that this should be corrected, there is no reason why more efficient hospitals should be geared to the administrative resources of the less efficient.

I am constantly amazed at the failure of the medical organisations to recognise that times have changed. With

the advent of effective treatments, and the great increase in numbers of the medical profession, the days of the patriarchal physician-superintendent, like those of the patriarchal general practitioner, are past. The necessity for playing such a part is happily over, and the way is open for the B.M.A. and the R.M.P.A. to prove how statesmanlike they can be in recommending a new form of mental-hospital administration.

Coulsdon, Surrey. JOHN T. HUTCHINSON.

DIRECTOR-GENERAL, N.H.S.?

SIR,—I think the *Journal of the American Medical Association*, as quoted by Colonel Walker last week, has got it wrong. At any rate, according to the definition that I heard, "a camel is a *horse* designed by a committee". The project, one gathers, was confided in the first place to the Planning and Development Subcommittee which after hearing a variety of views produced something like a dromedary. On presentation to the full committee, however, it was felt to be too dangerous so a second hump was added lest the rider should fall off. Later in the meeting the ears, which had been overlooked, were included under "Any Other Business". The tail, which had been completely forgotten, was added some days later by "Chairman's Action".

Medical Press,
8, Henrietta Street,
London, W.C.2. G. E. BREEN.

SIR,—I was extremely interested in your special article (Feb. 14) and also in the remarks of Colonel Walker last week. A little book of mine,[1] published in 1943, contains a table for the proposed new service administration. This commences as follows: "Director General and Council. Framing the policy for the medical services of the country and issuing instructions to carry out this policy." Had the ideas put forward in that little book been given favourable consideration there would now be no need for the remarks made by Professor Perry on Jan. 12.

Worthing. HAROLD LEESON.

END-TIDAL AIR SAMPLER

SIR,—Dr. L. H. Capel and Dr. D. C. Hodgson suggest in their letter last week that, if the tidal volume is large enough, the instrumental deadspace is washed out effectively. I wonder if one can be at all sure of this.

Some years ago, Dr. C. White and I made a careful comparison of the CO_2 content of end-expiratory with Haldane-Priestley samples,[2,3] and decided that velocity of air-flow was an important factor in washing out respiratory and instrumental deadspace. We designed a simple vacuum method, using a rubber bulb, which virtually excluded the instrumental deadspace and also the time factor, and only then obtained comparable results, later also including arterial-blood values.[4]

The misleading fact seems to be that a large tidal volume has a higher CO_2 content towards the end of expiration, since it represents the equivalent of longer breath-holding than is the case with a smaller tidal volume. Haldane himself was aware of this, and felt that samples collected by his method were often too high in CO_2 because of this concealed "breath-holding". The inexperienced donor of "Haldane-Priestley" samples of alveolar air generally goes far beyond the normal end-expiratory pause to provide the sample, because he has some confused idea that gas from the deepest parts of the lungs will be of a more representative composition, and in fact some of the textbooks actually encourage him to make this error. A short and sharp expulsion, the volume-equivalent of a small tidal air, appears to give the most accurate results as, in addition to keeping the time down, it effects a mechanical clearance of the deadspace.

Therefore it seems that mechanical end-tidal samplers can never give highly accurate results unless there is either trained cooperation from the patient, or alternatively some device for instantaneously washing out the deadspace before the sample is collected.

East Hoathly,
Sussex. C. A. FORSSANDER.

1. State Medicine or What; p. 11. High Wycombe, 1943.
2. Forssander, C. A., White, C. *J. appl. Physiol.* 1949, **2**, 110.
3. Forssander, C. A. *ibid.* p. 175.
4. Forssander, C. A. *ibid.* 1956, **8**, 509.

AN IMMUNOLOGICAL PUZZLE

SIR,—Having read your leading article last week I entirely agree with the views expressed by Mr. Fan in the same issue. The looseness of language of which he complains is shown by the following words in the leader: "Witebsy immunised rabbits with thyroid extract prepared from other rabbits."

Immunity, as Mr. Fan indicates, is decreased susceptibility to disease. It used to be taught that it is conferred naturally or artificially, actively or passively. Taking the above sentence out of context, exactly what does it mean? It *should* mean the rabbits obtained decreased susceptibility to a known disease by the injection of thyroid extract as the antigen—i.e., an artificially produced active immunity. Taken in its context the sentence means nothing of the sort, and Mr. Fan's "auto-antibodisation" is technically the correct term for the whole process described, including the rabbit response.

Agreeing with Mr. Fan that this is tongue twisting, I suggest an alteration to his earlier term—auto-antibody-production, or A.A.P. I should also like to suggest the word antigenated to mean the injection of an antigen which will produce an antibody where we are not speaking of specific immunisation.

The above sentence would then read: "Witebsky antigenated rabbits with thyroid extract prepared from other rabbits." The reader then knows that we are not dealing with an immunisation of the rabbits, but with antigen-antibody reactions and nothing more.

Finally, if we use the term auto-antibody-production (or A.A.P.) instead of auto-immunity, the process causing it can be called auto-antigenation, where the auto-antigen is part of the body substance produced by *any* cause.

Thus Witebsky antigenated rabbits with an external-auto-antigen (thyroid). This resulted in auto-antibody-production against this and the same internal-auto-antigen. This fully describes what he did in a few words and does not mislead with the mention of "immunisation".

Rayleigh, Essex. B. H. GOOCH.

PATHOGENESIS AND TREATMENT OF ENDOCRINE EXOPHTHALMOS

SIR,—After reading Sir Russell Brain's illuminating paper (Jan. 17) I am prompted to make an observation on a mechanical factor in the cause of the exophthalmos that is apt to develop in its later phases, and to mention certain indications for surgical decompression of the orbit.

Should natural processes or endocrine treatment satisfactorily control the degree of protrusion of the eyeball, all well and good; if not, then surgical decompression of the orbit should not be delayed.

The first sinister sign is œdema of the conjunctiva. Undoubtedly, the first phase in the mechanics of the exophthalmos is enlargement of the extraocular muscles, but in the later stages a vascular mechanism is superadded. In severe cases the orbital veins become strangulated at the sphenoidal fissure with ensuing venous engorgement and œdema.

In such cases decompression is imperative if the eyeball is not to be lost, and to get a satisfactory result it may be necessary to relieve the venous strangulation by removal of the upper margin of the sphenoidal fissure. Also, persistent discomfort

in the eye is common, even in medium degrees of exophthalmos, and in my experience this feeling of grit in the eye has nearly always been satisfactorily relieved by decompression of the orbit.

My colleague, Mr. Patrick Clarke, and I have found the lateral approach to the orbit to be the most satisfactory.[1]

Newcastle General Hospital. G. F. ROWBOTHAM.

DEATH OF A TESTICLE

SIR,—There is a dispute between Mr. V. J. Downie (Feb. 14) and Mr. Hamilton Bailey (Feb. 21) which can be settled only by agreement on a definition of "gangrene". I recently had occasion to examine the different senses in which this ancient word is used, and came to the conclusion that it is best defined as "tissue death combined with putrefaction".[2] This implies the entry of organisms into the affected tissue; but the appearance of discoloration would not in itself signify gangrene, because it could be produced by the decomposition of hæmoglobin (as in a bruise) without bacterial action.

London, S.W.15. K. W. LOVEL.

WEIGHT CHANGES IN INFANTS OF DIABETIC MOTHERS

SIR,—As exemplified in your leading article,[3] a diet short of carbohydrate (e.g., a high-fat diet) will induce weight-loss at least for some days. A substantial part of this loss is due to water excretion. While there is agreement on the existence of this initial dehydration on a diet low in carbohydrate, there seems to be no good explanation for this characteristic feature. Thus, Passmore et al.[4] put it in this way: "Perhaps the adult body may require 2–4 litres more body water whilst metabolising carbohydrate rather than fat." Studying the newborn infants of diabetic mothers we have met with like problems.

During intrauterine life the nutrition of the fœtus consists of carbohydrate. At delivery the glucose supply is cut off, and the infant loses weight for the first days, the respiratory quotient decreasing at the same time. The infant of a diabetic mother has had more glucose during intrauterine life, is longer and heavier at birth, and loses more weight during the first neonatal days than the normal infant. The output of urine is larger in such infants.

In the infants we have studied the total water content, the distribution of water in intracellular and extracellular compartments, and fat content, besides neonatal weight-loss, diuresis, &c. We found that the overweight is due primarily to fat. As in fat adults the total water content of infants of diabetic mothers is *low*, but the intracellular water is relatively *high*. The weight-loss and diuresis during fasting are greater than in control infants.

Our interpretation is founded on the investigations of Forsgren.[5] He compared the weight of rabbit livers with their glycogen content and found that 1 g. of glycogen by deposition binds 3·3 g. of water. The explanation of the findings in newborn infants of diabetic mothers runs as follows:

The constantly high glucose supply during pregnancy augments the deposits of glycogen and fat. Thus, the newborn infant is overweight, is fat, and has a relatively high intracellular water content in connection with glycogen. The newborn infant consumes first glycogen (as do normal infants), the bound water is excreted, and this explains the great diuresis and weight-loss. When the glycogen depots are nearly exhausted, fat is combusted. During the whole time protein is broken down as necessary.

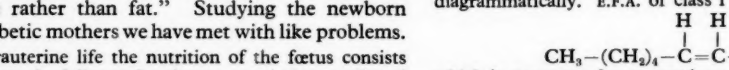
It seems to us that the glycogen-water deposits should be given due consideration in the explanation of the changes in weight and water in adults shifted from diets rich in carbohydrate to high-fat diets and vice versa. In our view it would be desirable to learn something about the carbohydrate stores of fat persons.

Royal Maternity Department B, Copenhagen. MOGENS OSLER JØRGEN PEDERSEN.

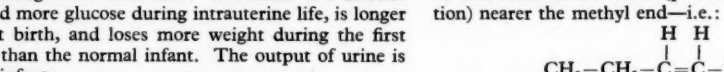
SUPPLY AND DIETARY USE OF FATS

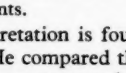
SIR,—Dr. Ahrens (Feb. 7) seems to hide very gracefully behind a "classical definition" of essential fatty acids (E.F.A.), though this (I believe) is to be found nowhere in the literature, and Surgeon Captain Cleave (Feb. 14) less gracefully behind the laws of Nature of which he appears to have the only extant tablet. If a few errors of fact are corrected, some clarity may ensue.

Dr. Ahrens' "classical definition" of E.F.A. is untenable. For him E.F.A. are those fatty acids that "satisfy certain metabolic requirements for growth"; they also prevent dermatitis, for instance, in rats. But those particular fatty acids that fulfil the first category do not necessarily fulfil the second: the usual form of linolenic acid (C_{18} with three double bonds) permits growth in rats on a fat-free diet but will not prevent dermatitis, and it does not have the chemical characteristics that Dr. Ahrens states are required for E.F.A.-activity. In fact for the rat we undoubtedly have a narrow class of E.F.A. that prevent a dermatitis and a wider class that permit growth; I believe this second class, probably widened further to include other fatty acids, prevents the deposition of lipid in rats fed a diet high in non-E.F.A. with some cholesterol, and if this deposition affects the health of the rats then for them these fatty acids must be regarded as essential. We can put this diagrammatically. E.F.A. of class I must contain the structure



which is necessary for preventing a dermatitis of rats. E.F.A. of class II comprise class I together with those that also include an additional double bond (probably also of the *cis* configuration) nearer the methyl end—i.e.:



Class I includes linoleic acid (found plentifully in most vegetable-seed oils) and arachidonic acid (which has two additional double bonds towards the right-hand side); fish-oils are poor sources of these two and do not in general prevent the dermatitis in rats. Class II includes linolenic acid and some highly unsaturated fatty acids found in certain fish-oils; these permit growth in rats on a fat-free diet. Certain other highly unsaturated fatty acids, such as the *trans* ( ) or conjugated () isomers, neither permit growth nor prevent the dermatitis although they contain the same number of carbon atoms and of double bonds as acids that do so. And the present evidence indicates that some at least of these isomers (e.g., in tung oil, which has conjugated linolenic acid or eleostearic) raise serum-cholesterol and produce atherosclerosis in rats under conditions in which the fatty acids of classes I and II lower serum-cholesterol and do not produce atherosclerosis.

What is true for the rat may or may not be true for man, and no-one should define E.F.A. for man in terms of E.F.A. for the rat. Rose's classical work on essential aminoacids for the rat was followed later by his careful experimental work on man which showed that the requirements were not identical; this in no way altered the definition of an essential aminoacid, just as the "classical definition" of vitamin C did not have to be

1. Rowbotham, G. F., Clarke, P. R. R. *Lancet*, 1956, i, 403.
2. Lovel, K. W. *Proc. R. Soc. Med.* 1958, **51**, 962.
3. *Lancet*, 1958, ii, 785.
4. Passmore, R., Strong, J. A., Ritchie, F. J. *Brit. J. Nutr.* 1958, **12**, 113.
5. Forsgren, E. *Svenska Läk. Handl.* 1935, **61**, 25.

altered when it was found that this was not a vitamin for the rat. I still support therefore my definition of E.F.A. given in 1952. But I am delighted to note that in his letter Dr. Ahrens has left behind in New York his "net-unsaturation" hypothesis (which means of course that the number of double bonds is the relevant factor and not their distribution or configuration); having arrived in this country he indicates in his last paragraph that he may accept the relevance of structure of the double bonds. If so, we are so near agreement that our differences could be settled over a pint of beer.

But not so with Surgeon Captain Cleave, for this unnatural drink is presumably taboo for him. The sunflower comes, he says, from the New World, and we of the Old World are not adapted to it and must have no truck with "these extraordinary and most unnatural substitutions"; mutton and beef fats are "wholly natural materials to us in these islands". This is historically wrong. The sheep has existed in England for not more than a third of man's existence here; the domesticated sheep was imported from Asia. It was introduced into Australia at the end of the 18th century and by the Phœnicians into Spain, where it may eat the sunflower seeds locally grown and its fat may then contain the fatty acids of the seeds; how "natural" will then be its fat as food for us? Similarly the cow was domesticated and brought here; under Dr. Cleave's definition its milk is unnatural—which is perhaps supported by the belief of the Samoans that if Nature had intended man to drink clean milk She (or It?) would have put the udder in the bows rather than in the stern of the animal. Surgeon Captain Cleave, in his book on *Fat Consumption and Coronary Disease*, which, though published in 1957, does not mention work such as that of Kinsell or Ahrens, contends that "the cause [of coronary disease] is eating fats for which the individual is not hungry". I cannot comment on this adequately because I do not know what it means; for him butter is apparently acceptable because allegedly "natural" whereas margarine is unacceptable because allegedly "unnatural", yet neither instinct nor hunger nor taste may differentiate the two for him. Whether under given conditions in man a fat raises serum-cholesterol (as does butter or mutton- or beef-fat) or lowers it (as do most vegetable-seed oils) is an experimental fact unaffected by Dr. Cleave's views on Nature.

In general, unprocessed fats are preferable to processed, but bacteria process fats in the rumen of cows and sheep, and margarine can be a better source of E.F.A. than is butter. It is essential that we should improve most foodstuffs to make them more digestible and less perishable, and cooking is one method of improving on Nature. Only by research can we tell whether our methods of processing are desirable or dangerous to health; instinct will not tell us.

Oxford. H. M. SINCLAIR.

DUODENAL-STUMP FISTULA

SIR,—Mr. Chambler is to be congratulated on his most valuable remarks on the management of duodenal-stump fistulæ.[1] He has clearly shown that in such cases, if the patient lies in near-vertical position on his left side, this will help to keep the stump and fistula dry. I have, so far, been lucky in not having a burst stump. But whenever I have had reason to fear that the closure of a stump has been precarious, I have kept the patient lying on his left side for about a week, with the head of the bed well raised. Mr. Chambler's anatomical explanation does seem to corroborate the logic of this; and I submit that the absence of this dreaded complication, even in those unavoidably poor closures of stumps that I have had, makes it a useful post-gastrectomy nursing hint. Suction, of course, helps also.

Patients, especially the stout ones, find the left lateral position quite uncomfortable on the left shoulder. A rubber-ring pillow housing the convexity of the shoulder will be found to give relief.

1. Chambler, K. *Lancet*, 1958, ii, 1303.

Glace Bay, Nova Scotia, Canada. S. W. A. GUNN.

GOWN AND GLOVE DRUMS

SIR,—May I draw attention to a defect in the drums used for sterilising gowns and gloves? The clasp of the lid is so placed that the contents are liable to become contaminated, and the clasp may be strained when the lid is dropped to the closed position. It has occurred to me that, if the clasp were reversed, contamination and straining would be avoided.

Memorial Hospital, Peterborough. D. W. BRACEY.

CHILDREN IN HOSPITAL

SIR,—Dr. David Lawson is not entitled, as he did in his letter last week, to isolate para. 34 and use it to suggest that members of the committee under my chairmanship wished to see the abolition or breaking up of children's hospitals—whether short-stay or long-stay institutions. This accusation simply will not hold water. What the committee had to take note of was the fact that since the advent of the National Health Service a number of new consultant pædiatrician appointments had been made to general-hospital groups in the regions, and that the units allotted to them were for the time being quite small. This is a problem in hospital structure. Obviously, by taking children out of adult wards, where accommodation is available such units can give a fuller service to catchment areas which are not served by large children's hospitals. Nevertheless, the committee felt that the measures of welfare which they commended could and should be adopted in quite small children's units. They were also fully aware that some of our famous children's hospitals had already given a lead in this matter.

As to the chronological relation of the publication of the report to the debate in the House of Lords, and Lord Cohen's remarks on the larger strategy of hospital policy, Dr. Lawson is again letting his imagination run riot. But this is not my affair, and my friend Lord Cohen is admirably equipped to deal with such situations.

Having said this, I would say that I am one who sympathises with Dr. Lawson's natural anxiety about the future of his own hospital in the larger world of children's medicine. I knew Queen Mary's Hospital in its heyday as a long-term orthopædic centre under the late Dr. W. T. Pugh. But those of us who have been responsible for the care of the physically handicapped child for the past forty years have witnessed a veritable revolution. Today the need for hospital accommodation for such children is small. What is still needed, however, and will be needed for some years to come, is a second line of defence—not more beds in *wards* of residential hospital-schools, but beds in *dormitories* in special boarding-schools for those seriously handicapped children who, after the fullest possible hospital rehabilitation, cannot conveniently attend day schools. Such schools (and many now exist) must also provide for children with special educational needs—e.g., the spastic group. Thus what in the early phase is a health problem becomes predominantly an educational problem; and still later a vocational training problem. The physically handicapped child looks to three Ministries as his godfathers—Health, Education, and Labour.

Manchester. HARRY PLATT.

SIR,—I feel that I must reply to the disparaging attack on infectious-disease hospitals concerning their treatment of gastroenteritis patients, made in your leading article of Feb. 14.

Firstly, it is stated that laboratory facilities in these hospitals are inadequate or non-existent. Nowadays, even the largest hospitals seldom possess complete laboratory resources, owing to the development of newer and more exacting techniques, such as those concerned with virology. However, in so far as the laboratory facilities in infectious-disease hospitals are incomplete, they are supplemented by the full resources of the other laboratories of the hospital group to which they belong, including a 24-hour service of laboratory technicians, and by the Public Health Laboratory Service.

Secondly, in regard to medical staff, I suggest that a doctor working in infectious disease only can devote more time and attention to gastroenteritis patients and have greater experience in their treatment than a doctor who covers the full field of pædiatrics. Nor does our mortality-rate suggest that our treatment of these patients is inadequate. During the year 1958, for instance, I had no death among the total of 60 cases of gastroenteritis treated. I apologise if this may seem boastful, and hasten to add that I have no doubt that those of my colleagues who are working in larger infectious-disease units could produce even more impressive statistics from the larger numbers of patients they treat. I must also acknowledge with gratitude the invaluable help given by nursing staff who have long and constant experience in the treatment of gastroenteritis.

Finally, I fail completely to see the relevance of " lack of educational facilities " in this context, since it mainly concerns babies suffering from an acute illness. In my experience, it is very rare for a child of school age to have to be admitted to hospital for gastroenteritis, and in the few we do admit recovery is rapid.

Waddon Hospital, Croydon. J. J. LINEHAN.

SIR,—In your leading article you ask if the day will come when a child will be occasionally allowed to visit his sick parent in hospital. An inquiry would, I think, show that it has come in some places.

Here, where we deal mainly with tuberculous patients, visiting by children was introduced about three years ago, at first cautiously and by now a little more freely. Before a visit is allowed, it is established that the child has been tuberculin-tested and vaccinated with B.C.G. if negative. The child is not allowed to come during ordinary visiting periods, but the parent and ward sister arrange another suitable time and the meeting takes place in a room away from the wards. The degree of contact encouraged or discouraged depends on the phase of the parent's disease, and on many occasions it is considered desirable for a nurse to be present the whole time. I feel confident that no child has come to harm by this arrangement. Facial expressions alone suffice to indicate the joy the visits bring.

One difficulty in treating tuberculous patients is that some leave hospital against advice with their disease uncontrolled. It is from this group that patients often drift to form the hard core of problem cases, with persistent cavitation and drug-resistant tubercle bacilli. Separation from children is one important factor in producing the unsettled state that leads to self-discharge. Visiting was introduced not only to reduce this but also to relieve the pangs felt by many who would not take such an extreme step. The delight of the child is often as great as that of the parent.

Because tuberculosis is a family disease, we often have a parent and child in hospital at the same time. Prohibition of visiting is then even less justified, and we allow it fairly freely. An endeavour is always made to have both parent and child in the same hospital. It is sad to relate that the only obstacle—with unfortunate effects on the mother—has come from a children's hospital whose staff have written ably on the emotional needs of the child in hospital. The reason given was that the child recovering from tuberculous meningitis needed to be in a special unit.

I believe, Sir, that it will now do us good to hear more of the emotional need of the parent who spends a long time in hospital.

Ransom Hospital,
Rainworth, near Mansfield, Notts. D. DAVIES.

" NORMAL MIDWIFERY "

SIR,—Mr. FitzGerald, in his article last week, states that, after consultant screening, the perinatal mortality in one of the maternity-homes fell from 32·4 to 12·7 per 1000. It would be interesting to know whether the corresponding figures for the hospitals to which patients were transferred showed a rise or a fall.

Clitheroe, Lancs. J. ROBERTS.

Parliament

Royal Free Hospital

ON the adjournment on Feb. 20 Mr. MICHAEL CLIFFE raised the question of the proposal to close the Royal Free Hospital and the Elizabeth Garrett Anderson Hospital and to move these hospital services to Hampstead. Mrs. LENA JEGER welcomed the news that London was to have a new teaching hospital at Hampstead, but asked whether this must automatically mean the closing of the other buildings. The Elizabeth Garrett Anderson Hospital met the need of many women who felt unable to go to our big teaching hospitals for an intimate examination at which they might be surrounded by hordes of young men students. She reminded the House that there was a large daytime population in the area, that over half the admissions to the Royal Free Hospital were emergency admissions, and that the outpatient department was near the main-line termini.

Mr. RICHARD THOMPSON, parliamentary secretary to the Ministry of Health, said that the decision to rebuild the Royal Free Hospital at Hampstead, on the site of the Hampstead General Hospital and the North Western Hospital, was founded largely on the recommendations of the Goodenough Committee on Medical Schools, which reported in 1944, and the London Hospital Survey of 1945. This recommendation was made in view of the likely decline in population and what was considered to be the over-concentration in the London area of medical schools with their associated hospitals. When the National Health Service was set up the Royal Free, the London Fever, the North Western, the Elizabeth Garrett Anderson, and the Hampstead General were designated as a teaching group with the long-term aim of rebuilding the Royal Free at Hampstead. When the new hospital had been built the intention ultimately was to close the Royal Free Hospital, the London Fever Hospital, the Elizabeth Garrett Anderson Hospital, and the New End Hospital at Hampstead. But the problem would need a great deal of further study. If all went well, a start would be made on the Royal Free Hospital in 1960–61. The project would take several years to complete, because the building would have to go on while the hospital was continuing to give full service to patients. It was too early now to be thinking in terms of taking final decisions on closures. The Ministry had to indicate a general policy, but their minds were not closed. They must see what progress they made and what the needs of the future turned out to be.

Hospital Waiting-lists

ON Feb. 23 on the adjournment Mr. ARTHUR BLENKINSOP raised the question of hospital waiting-lists, with special references to the difficulties of North-East England. In that area, he said, patients might have to wait 5–6 weeks for an appointment with a consultant, and there had been many

complaints that the most reliable way to secure an early consultation was by paying for it. Mr. Blenkinsop was satisfied that an urgent case was seen and admitted to hospital reasonably quickly. But problems arose in the definition of " urgent ", and he had gained the impression that private consultation was on the increase and was being encouraged by the long waiting-lists. He suggested therefore that a real effort should be made to improve the staffing position. Specialist recruitment in the Newcastle R.H.B. area had been rapid in the early days of the N.H.S., rising from 164 specialist appointments in 1948 to 370 in 1953. But since then the speed had slackened, and in the years 1954–57 there were only 21 new appointments.

Turning from the waiting periods for consultations to the waiting periods for beds, he was perturbed that in the Newcastle region waiting-lists had lengthened since 1955. General surgery and gynæcology were the specialties where admission was most difficult. The accommodation in the region for psychiatric and geriatric cases was also inadequate. He asked the Minister, after consultation with the hospital authorities, to review the needs of the area for more consultants and beds. In his view the Ministry had for too long been unwilling to exert leadership and pressure.

Dr. EDITH SUMMERSKILL thought that too many people on the waiting-lists were dismissed as patients with " chronic conditions ", with the implication that it did not matter that they had to wait. It was inhuman that a man with a hernia or a woman with a prolapsed womb should have to carry on working without treatment.

Mr. THOMPSON said that in the Newcastle area the number of patients awaiting hospital treatment was about the same as the national average of 1% of the population. The region had entered the N.H.S. with a handicap, for its hospital facilities were relatively limited and sometimes below acceptable standard. Allowance had been made for this, and the region had always had more than its share of capital money, reckoned on a strict population basis. He agreed that there had been some fluctuation in the waiting-list figures, but he said that this was marginal and under control. The picture would improve as the facilities to be provided by the nine centrally financed building schemes came into operation.

QUESTION TIME

Treatment of Mental Patients

Mr. P. W. SORENSEN asked the Minister of Health if he was aware that, in a recent television broadcast by the British Broadcasting Corporation, an ex-patient of a mental hospital made charges of violent and brutal treatment of patients, which he had witnessed; and if he would request the Corporation to supply him with the script of the broadcast, with a view to taking such further steps as might be necessary in consultation with the British Broadcasting Corporation and the hospital board concerned in order to maintain public confidence in the mental health services.—Mr. DEREK WALKER-SMITH replied: I have asked for and received the script from the B.B.C., and I am in touch with the director-general about certain questions arising on this programme. In order that full inquiries may be made, I have asked to be given full particulars of the incidents referred to in the programme in question. Further action must, of course, await their receipt.

Dr. EDITH SUMMERSKILL: Is the Minister aware that it is not unusual for ex-mental patients to make allegations of this kind against nurses who work in mental homes where they are often among the finest in the nursing profession, being called upon to do uncongenial work and at all times to restrain their tempers? In view of that, will he make strong representations to the B.B.C. that under no circumstances should it sensationalise this tragic illness, mental illness, because on such occasions patients in mental hospitals all over the country watch the incident and it is neither in their interests nor in those of the nurses that the B.B.C. should make cheap propaganda on television in this way?—Mr. WALKER-SMITH: The Corporation is already in possession of my views on this matter, and, in particular, as to how unfortunate it would be if a programme of this sort deterred someone from seeking mental treatment when he would otherwise have done so. I should say in fairness to the British Broadcasting Corporation that hitherto it has done a lot to help to foster a balanced public view of the importance of mental disorder. I wholly agree with what the right hon. Lady has said about nurses and others working in our mental hospitals. They work under very difficult conditions, and I am sure that the whole House would join in a tribute to their work.

Part-time Consultants

Mr. D. H. HOWELL asked the Minister whether he was aware of the growing concern regarding the transfer of consultants and specialists in the health service from whole-time to maximum part-time employment; who was responsible for supervising such employment; why he had directed that a legal opinion to the effect that such a transfer constitutes new conditions of service and should be treated as a new contract should be disregarded; and why he was encouraging the automatic transfer of these consultants.—Mr. WALKER-SMITH replied: These doctors are appointed and employed by regional hospital boards and boards of governors. I am advised that where there is no substantial change in duties there is no need to advertise the post when the contract is varied by the parties. I am in no way encouraging the automatic transfer of consultants to part-time employment; such transfers are a matter for local arrangement.

Cost of Drugs

Mr. E. G. FLETCHER asked the Minister of Health on what grounds he had satisfied himself that prices for corticosteroids which operated until July, 1958, at which period identical prices had been submitted to his Department for almost all items in this group during the previous two years, were fair and reasonable, in view of the drop from £56 to £12 per 1000 tablets for one item of prednisteroids during the four months subsequent to July, 1958; whether he was aware that this price reduction was by stages which were all observed contemporaneously by the leading American-owned or American-licensed companies in the United Kingdom; and whether he would reconsider his decision not to hold an inquiry.—Mr. WALKER-SMITH replied: Progress of manufacture has been closely watched with a view to securing reductions in price where possible, but initial costs were very high and no substantial reductions could be anticipated until economic production had been obtained. I am informed that, since July, 1958, uniform prices have not obtained. I see no need for an inquiry.

Mr. MAURICE EDELMAN asked the Minister whether, notwithstanding that his Department did not normally purchase raw materials for the preparation of ethical drugs, he would make inquiries, in the course of his regular investigations into manufacturing costs where monopoly patents apply, as to the charge made by an American company's subsidiary operating in the United Kingdom, of 40*s*. per hundred 10 mg. tablets of mecamylamine hydrochloride in view of the fact that this material was available in Europe at £100 per kg. and that the profit on the price to the National Health Service, after allowances for manufacturing costs, was approximately 990%. —Mr. WALKER-SMITH replied: I understand that this drug is classified by the Standing Joint Committee on the Classification of Proprietary Preparations as a new drug of proved value not yet standard, and its price is therefore not regulated at present by the scheme agreed with the pharmaceutical industry.

Deaths from Leukæmia

Mr. FRANK ALLAUN asked the Minister of Health what were the causes of the rise in deaths from leukæmia in Lancashire by 22% between 1950–53 and 1954–57, and by 40% in Cumberland, compared with 13% for the whole of England and Wales.—Mr. WALKER-SMITH replied: The increases illustrate a recent narrowing of the gap between the death-rate from leukæmia in the north of England and the higher rate in the south. This trend may well be due in part to greater accuracy in diagnosis.

Sterilising Techniques

Mr. B. R. BRAINE asked the Minister what action he was taking with regard to the report of the operational research team of the Nuffield Provincial Hospitals' Trust, which revealed that the sterilising techniques employed in the six hospitals covered by the team's inquiry were inadequate and that this was contributing to the present high incidence of hospital infection.—Mr. WALKER-SMITH replied: The report has been widely publicised and is by now well known to hospital authorities. In addition, the attention of the senior administrative medical officers of regional hospital boards has been specifically drawn to it; and in allocating sums to those boards for their revenue expenditure in 1959–60 I have asked them to have regard to the report in determining their expenditure. I shall similarly draw the attention of boards of governors of teaching hospitals to this matter within the next few days.

United Nations Children's Emergency Fund

Baroness ELLIOT OF HARWOOD asked why no expert in child welfare was sent to meetings of the executive board of this Fund, as it appeared to be the custom in other agencies of the United Nations, such as the World Health Organisation, United Nations Educational, Scientific, and Cultural Organisation, and Food and Agricultural Organisation for experts, both official and non-official, to be sent. The Earl of HOME replied: My Lords, the composition of the United Kingdom delegation at meetings of this kind, whether of the board of UNICEF or of any other United Nations body, depends on the agenda of the meeting concerned. When the agenda require the presence of experts, they are sent. When, however, individual technical items are not sufficiently important in themselves to justify the expense of sending experts they are dealt with by our representatives on the basis of briefs prepared beforehand with the necessary technical advice. On this occasion, however, Prof. A. A. Moncrieff has accepted the Government's invitation to join our delegation to the forthcoming meeting in Geneva.

Leprosy

There are 279 cases of leprosy in this country at present.

Obituary

HUGH MICHAEL DENNE SHEPHERD

M.D. Edin., F.R.C.P.E.

Dr. Hugh Shepherd, physician to the Dudley Road Hospital, Birmingham, died on Jan. 18.

He was born in 1907 and was educated at Glenalmond, University College, Oxford, and the University of Edinburgh where he qualified in 1932. He settled in general practice at Shanklin in the Isle of Wight. During the late war he served with the R.A.M.C., and, with the rank of lieut.-colonel, he was in charge of a medical division in Iraq. On his return to civilian life he decided to give up general practice, and after holding a post as R.M.O. at Redhill Hospital, Edgware, he took up his consultant appointment in Birmingham.

K. M. writes:

"Hugh Shepherd's mind was methodical and logical, and diagnosis for him was a matter of precision. He was imaginative, but he detested loose speculation in medicine. The newest therapy commanded his interest, but conviction only followed searching personal trial. His work covered the gamut of medicine, but his especial interest was rheumatology and crowded clinics bore witness to his success. Each patient received the same unhurried care, and was finally given a verbal summary suited to his understanding which sent him away convinced that 'the doctor understands my case'. Shepherd's methodical mind was evident in the committee room, and many a meeting was shortened by his ability to select relevant matter from diffuse contributions. To his residents he was an example: to his colleagues, once a crust of shyness had been penetrated, he was a stimulating companion and a true friend."

Dr. Shepherd leaves a widow and two sons.

THOMAS JAMES BERRY ARNOTT MacGOWAN

Ch.M. Glasg., F.R.C.S., F.R.C.S.E.

Mr. MacGowan, consultant surgeon to the hospitals in the York A group, died at his home on Jan. 29 at the age of 50.

After graduating M.B. from Glasgow University in 1931 he did postgraduate work at the Royal National Orthopædic Hospital, London, and at the General Hospital, Birmingham. During the late war he was an orthopædic specialist in the R.A.F., and at the end of the war he came to York as an orthopædic surgeon.

A colleague writes:

"MacGowan was a man with abundant physical energy, and with apparent ease saw and treated vast numbers of patients whom he always seemed to know individually, and who trusted him implicitly. He was a natural collector—a collector of fine antiques and of many other things of interest, such as unusual but apt surnames. One of his most treasured possessions was a 16th-century house, and he had himself restored much of the fabric and contents, for he had a knowledge and feeling for wood and was as much a master of techniques in that medium as he was with human tissues.

"He was also a brave man. Knowing for several months that his life could only be short, he continued to work, and even in this period his sense of humour remained unchanged."

Mr. MacGowan leaves a widow, one son, and three daughters.

RUSSELL VYVYAN STEELE

M.B., Durh.

Dr. Russell Steele, who was in general practice for many years at Gloucester Gate, London, died suddenly on Feb. 9 at the age of 70.

He was born at Hemel Hempstead, the fourth in a line of general practitioners. He was educated at Epsom College, where his father had been one of the first pupils, and at University College Hospital, London, and the College of Medicine, Newcastle upon Tyne, where in 1913 he graduated M.B. After holding house-appointments at the West London Hospital, he was appointed resident surgical officer of the Schiff Home of Recovery, Cobham, when the first Belgian wounded and casualties from the B.E.F. were being admitted. Later he served with the R.A.M.C. in France and at Salonika. In 1919 he settled in general practice at Devizes, Wilts, and three years later he came to London to practise at Gloucester Gate. For over thirty years he took an active part in the work of the St. John Ambulance Brigade, and he became area commissioner of Central Area. In 1951 he was made a knight of the Venerable Order of St. John of Jerusalem. Latterly he took great interest in the Legion of Frontiersmen, of which he was chief medical officer. He was a freeman of the City of London, a yeoman of the Society of Apothecaries, and a member of the Royal United Services Institution.

A colleague writes:

"Russell Steele was a man of many interests and had a good knowledge of several languages in which he corresponded on military history and military uniforms, on which he was an authority. He was a member of the Army Historical Research Society, and he was the author of many articles on the history of military uniforms. The walls of his consulting-room are covered with a fine collection of old coloured military prints, including four very fine specimens presented to him on his retirement from the St. John Ambulance Brigade. He was well known for his rapid pen-and-ink sketches, and rarely wrote a letter without embellishing it with a military sketch.

"He was a great opponent of 'State medicine', believing that a doctor should be free as an individual and responsible only to his patients. In this he was upholding the tradition handed down to him by his greatgrandfather. As one of his patients said: 'Dr. Russell Steele was one of the old school—a true friend to his patients and much beloved, and he will be sadly missed'."

Notes and News

PROF. H. R. DEAN'S 80th BIRTHDAY

IT is seldom in these days that the occupant of a chair in a medical faculty of a university reaches the age of 80; but Dr. H. R. Dean, professor of pathology in the University of Cambridge, achieved this distinction on Feb. 19. He is the last of the Cambridge professors to hold his chair under the old statutes, by which there is no retiring age.

The occasion was celebrated by the past, present, and honorary fellows of Trinity Hall, of which Professor Dean was master for 25 years until he retired in 1954, at a dinner-party on Professor Dean's birthday, during which a piece of silver was presented to him by Sir Ivor Jennings, the master. The birthday is also to be celebrated by Professor Dean's colleagues in the department of pathology at Cambridge at a dinner-party at the end of February.

A MISSIONARY SURGEON

Sir Henry Holland graduated from Edinburgh University in 1899, and within a few months he set off to work in a missionary hospital on the North-West Frontier. During the next fifty years he lived in India or Pakistan, and won international fame as an ophthalmologist. But at no time was he ever concerned to use this reputation to gain wealth. He lived quietly and modestly, and he continued to think his work as a preacher at least as important as his work as a surgeon.

His autobiography [1] describes some unusual aspects of medical practice. In this country it is difficult to picture a population with so much disease and so few doctors, or a hospital that held in a single day 200 eye operations, about half for cataract. It is not surprising that ophthalmic surgeons came from all over the world to study Sir Henry's technique and to acquire the confidence that came from the opportunity to do hundreds of cataract operations during a visit of a few weeks.

Sir Henry's account of the Quetta earthquake disaster of 1935, in which 20,000 people died in less than thirty seconds, is impressive. But the most remarkable thing about his book is the spirit with which it is informed. When so many autobiographies seem to be written to gain prestige for their authors, Sir Henry's modest style and the faith which has been the strength of his whole career are peculiarly refreshing.

University of London

Mr. G. L. Slack, senior lecturer in preventive dentistry in the University of Liverpool, has been appointed to the chair of dental surgery at the London Hospital Medical College.

The following degrees have been conferred:

M.D.—A. S. Burgen, J. A. Dossett, J. L. Turk, D. L. Walker.
M.S.—John Whitwell.

University of Sheffield

Dr. W. A. J. Crane has been appointed senior lecturer in pathology and Dr. T. G. Kershaw lecturer in physiology.

University of Edinburgh

The status of honorary lecturer in the department of surgical science has been conferred on Dr. Willard E. Goodwin, professor of urology in the University of California.

Royal College of Physicians of London

On Tuesday and Thursday, March 10 and 12, at 5 P.M., at the college, Pall Mall East, S.W.1, Dr. P. L. Mollison will give the Oliver-Sharpey lectures. His subject will be blood-group antibodies and red-cell destruction.

Royal College of Surgeons of England

Faculty of Anæsthetists.—On Wednesday, March 14, at 4 P.M., at the college, Lincoln's Inn Fields, London, W.C.2, Dr. C. Langton Hewer will give the Frederic Hewitt lecture. His subject will be Forty Years On.

1. Frontier Doctor. By SIR HENRY HOLLAND. London: Hodder and Stoughton. 1958. Pp. 256. 25s.

University of Durham

Dr. C. A. Green has been appointed to the chair of bacteriology in the Newcastle division.

Dr. Green, who is 50 years of age, is at present lecturer in this department and clinical bacteriologist to the United Newcastle upon Tyne Hospitals. He qualified from the University of Edinburgh in 1932, and after holding an Empire Rheumatism Council research scholarship he was appointed senior lecturer in bacteriology in the University of Edinburgh. During the late war he served in the R.N.V.R. with the rank of surgeon commander. In 1941 he took the degrees of PH.D. and M.D. He took up his present post in 1947. His published work includes papers on hæmolytic streptococcal infections, acute rheumatic fever, and the production of penicillin.

Mr. G. L. Howe has been appointed to the chair of oral surgery.

Mr. Howe is 34 years of age. In 1946 he qualified L.D.S. R.C.S. from the Royal Dental Hospital of London and, after completing his military service he took the M.R.C.S. from the Middlesex Hospital in 1954. After holding house-appointments at the Middlesex he became registrar in oral surgery at the Eastman Dental Hospital (Institute of Dental Surgery) and obtained the F.D.S. R.C.S. in 1955. He was senior registrar at the plastic and oral surgery centre at St. Lawrence Hospital, Chepstow, before he returned to the Eastman Dental Hospital to his present post of senior registrar in the oral surgery department.

Royal College of Surgeons in Ireland

At a charter day dinner on Feb. 14 the honorary fellowship of the college was conferred on Sir Ernest Finch and Sir Archibald McIndoe.

On Feb. 20 the fellowship was conferred on Gearoid Lynch.

Walter W. Wright Lecture

This lecture has been established at the University of Toronto in honour of Dr. Walter W. Wright, who is professor emeritus of ophthalmology. The first lecture will be given on Feb. 27 by Prof. Norman Ashton, who will speak on A New Approach to the Problem of Diabetic Retinopathy.

Association of Psychiatric Social Workers

The annual general meeting of this Association will be held on Saturday, March 21, at 2.30 P.M. at the Overseas League, Hall of India, St. James', London, S.W.1. Dr. Alexander Walk will give a presidential address on the state of lunacy 1859–1959.

Association of Physicians of East Africa

This Association will hold its annual conference in Kampala from June 18 to 20. Further particulars may be had from the president, Dr. P. W. Hutton, P.O. Box 43, Nakasero Hospital, Kampala, Uganda.

Nutrition Society

On Saturday, April 4, in Glasgow, the Scottish group of this society will hold a symposium on obesity. Further particulars may be had from Dr. J. Davidson, The Rowett Research Institute, Bucksburn, Aberdeenshire.

European Association Against Poliomyelitis

A meeting of this Association will be held in Munich from Sept. 6 to 9. Further particulars may be had from Dr. W. Ritchie Russell, c/o Royal College of Physicians, 12, Pall Mall East, London, S.W.1.

International Congress on Irradiation of Endocrine Organs

This congress will be held in Amsterdam from May 30 to June 1. The speakers will include Dr. A. B. Wayte. Further particulars may be had from Dr. J. M. van Went, Banstraat 30 hoek de Lairessestraat, Amsterdam Z I, Holland.

Operation of Sterilising Autoclaves

A symposium on this subject will be held at Brighton Technical College School of Pharmacy, Richmond Terrace, Brighton, 7, on Saturday, May 9, at 10 A.M. The speakers will include Dr. J. C. Kelsey and Dr. J. H. Bowie. Further particulars may be had from Dr. J. C. Parkinson at the school.

Institute of Basic Medical Sciences

This institute will hold a course on genetics at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2, from March 2 to 6. Lectures will be given daily at 10 A.M. and 11.30 A.M., and the speakers will be Mr. J. Maynard Smith, Prof. Charles Dent, Dr. Harry Harris, Prof. Hans Grüneberg, Prof. L. S. Penrose, and Dr. J. A. Fraser Roberts. Further particulars may be had from the secretary of the Institute, Mr. W. F. Davis, at the Royal College of Surgeons.

British Society for the History of Science

To commemorate the centenary of the publication of the *Origin of Species* a symposium on Darwin, Evolution, and Modern Life will be held in the Wellcome Building, Euston Road, London, N.W.1, on Saturday, March 14, at 10.15 A.M. The speakers will include Dr. E. Ashworth Underwood, president of the society, who will read a paper on Darwin and the Doctors. Tickets (members 5*s.* 6*d.*, non-members 10*s.* 6*d.*) may be had from the hon. secretary of the society, Ravensmead, Keston, Kent.

The University of Cambridge Postgraduate Medical School will hold a course on metabolic aspects of disease from April 9 to 11, at the medical school, Tennis Court Road. Further particulars may be had from the secretary of the medical school.

The Faculty of Radiologists is arranging to hold postgraduate courses this autumn, starting in October. Further particulars will be found in our advertisement columns.

Dr. E. E. Pochin is to lecture on radioisotopes to Italian medical schools by arrangement with the British Council from March 3 to 19.

The price of the Joint Tuberculosis Council's report on the antenatal and obstetric care of tuberculous patients (see *Lancet*, Feb. 14, 1959, p. 354) is 9*d.*

The 1958 edition of the *Medical and Dental Directory of the London Hospital* has been published.

Mrs. Vera Colebrooke's play *Natural Causes*, which deals with euthanasia, will be given at the Arts Theatre, 6, Great Newport Street, London, W.C.2, on March 16, at 7.30 P.M.

Appointments

DAVY, B. W., M.D. Lond., D.P.M., D.P.H.: consultant psychiatrist, United Cambridge Hospitals.
DALLEY, VERA M., M.B. Lond., D.M.R.T.: consultant, radiotherapy department, Royal Marsden Hospital, London.
GHOSH, S. K., M.B. Calcutta: orthopædic registrar, King's Lynn group of hospitals.
GROVES, H. J., M.B. Lond., F.R.C.S.: consultant surgeon, E.N.T. department, Royal Free Hospital, London.
POLLOCK, ILSE, M.D. Wurzburg, L.R.C.P.E.: pædiatric registrar, Jenny Lind Children's Hospital, Norwich.
ROBERTS, D. P. W., M.B. Birm., D.OBST., D.P.H.: deputy M.O.H., Blackpool.
ROSS, A. I., M.D. Edin., D.P.H.: M.O.H. and principal school M.O., Bolton.
SIMMONS, C. A., B.M. Oxon., F.R.C.S., M.R.C.O.G.: consultant gynæcologist, Royal Marsden Hospital, London.
THOMAS, D. F., M.B. N.U.I., F.R.C.S.: part-time consultant orthopædic surgeon, Lincoln area hospitals.

South Western Regional Hospital Board:

HARRIS, R. H., M.B. Lond., D.P.M.: assistant psychiatrist, Digby-Wonford Hospital, Exeter.
PENCHEON, J. M., M.B. Leeds, D.P.M.: consultant psychiatrist, West Cornwall clinical area.
RODGER, WILLIAM, M.B. Cantab., D.P.M.: consultant psychiatrist, Exeter clinical area.

Welsh Regional Hospital Board:

ANDREWS, J. D. B., M.D. Lond., D.P.H.: consultant geriatrician, Merthyr and Aberdare, and Brecon and Radnor H.M.C. areas.
JONES, E. M., M.R.C.S., D.P.H.: consultant psychiatrist/medical superintendent, Ely Hospital, Cardiff.
JONES, J. G. P., M.D. Lpool, M.R.C.P., D.C.H.: consultant geriatrician, Caernarvon and Anglesey H.M.C. area.

Births, Marriages, and Deaths

DEATHS

WILLIAMS.—On Feb. 22, at Willesden General Hospital, Thomas Pearse Williams, M.D., F.R.C.P., of 7, Corringham Road, Wembley Park, Middlesex, aged 65.

Diary of the Week

MARCH 1 TO 7

Monday, 2nd

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Dr. Brian Ackner: Hysteria.
INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S.E.5
5.30 P.M. Dr. W. S. Feldberg: Physiological Approach to the Problem of Loss of Consciousness.
UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. H. B. Goodall, Dr. William Walker: The Megaloblastic Anæmias.

Tuesday, 3rd

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8 P.M. *Pathology and Radiology.* Dr. H. J. G. Bloom, Dr. R. H. Mole, Dr. A. Glucksmann: Changes Produced in Tissues by Irradiation.
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Prof. A. A. Miles: Mediators of the Vascular Phenomena of Inflammation.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Dr. Lars Bengtsson: Hormonal Control of Pregnancy and Labour in the Human.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. A. W. Frankland: Allergy and Dermatology.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Prof. F. C. Ormerod: Histochemistry of the Inner Ear.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Dundee.) Dr. A. C. Turnbull: Investigation of Uterine Contractility.

Wednesday, 4th

ROYAL SOCIETY OF MEDICINE
5.15 P.M. *History of Medicine.* Lord Cohen of Birkenhead: Richard Caton (1842–1926)—Pioneer Electrophysiologist.
POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. Robert White: Immune Cellular Reactions.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Miss B. M. Partridge: New Cultural Techniques for the Investigation of Pathogenic Fungi.
INSTITUTE OF DISEASES OF THE CHEST, Brompton. S.W.3
5 P.M. Dr. F. J. Prime: Factors Limiting Exercise Tolerance.
MIDLAND MEDICAL SOCIETY
8.15 P.M. (36, Harborne Road, Edgbaston, Birmingham, 15.) Mr. A. J. H. Rains: Life and Death of a Cholecystectomy.
MANCHESTER MEDICAL SOCIETY and LIVERPOOL MEDICAL INSTITUTION
5 P.M. (Medical School, University of Manchester.) Mr. Philip Hawe, Dr. W. H. R. Cook, Dr. William Kulke: Current Trends in the Management of Thyroid Disorders.
UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. Goodall: Hæmolytic Anæmia in Pregnancy.

Thursday, 5th

ROYAL SOCIETY OF MEDICINE
5 P.M. *United Services.* Surgeon Captain F. W. Baskerville, Surgeon Lieutenant P. C. Barrington, Surgeon Lieut.-Commander I. H. Colley, Surgeon Commander E. Boyd Martin: Aspects of Naval Aviation Medicine.
8 P.M. *Neurology.* Sir Charles Symonds: Excitation and Inhibition in Epilepsy. (Hughlings Jackson lecture.)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Prof. D. F. Cappell: Iron Metabolism.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
5.30 P.M. (Royal College of Surgeons, Lincoln's Inn Fields, W.C.2.) Mr. Robert Brain: Œsophageal Replacement.
ALFRED ADLER MEDICAL SOCIETY
8.15 P.M. (1, Wimpole Street, W.1.) Dr. A. Spencer Paterson: Use of Physical Methods in Psychotherapy.
WEST LONDON MEDICO-CHIRURGICAL SOCIETY, West London Hospital, W.6
8 P.M. Prof. Alexander Haddow: Chemotherapy of Malignant Disease.

Friday, 6th

UNIVERSITY OF LONDON
5.15 P.M. (University College, Gower Street, W.C.1.) Prof. J. Folch-Pi (Harvard Medical School): Brain Lipoproteins and Proteolipids. (First of two lectures.)
ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Otology.* Prof. Horst Wullstein (Wurzburg): Fundamentals and Tasks of Plastic Surgery in the Operations to Restore Healing.
2.30 P.M. *Laryngology.* Prof. D. V. Hubble, Mr. Harold Zalin: Respiratory Catarrh in Children.
5.30 P.M. *Anæsthetics.* Dr. Andrew Doughty: Evaluation of Premedication in Children.
POSTGRADUATE MEDICAL SCHOOL
10 A.M. Prof. A. W. Wilkinson: Principles in Neonatal Surgery.
4 P.M. Prof. W. S. Peart: Aspects of Carcinoidosis.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Dr. C. H. Edwards: Recent Advances Concerning Cerebral Vascular Disease.
JAMES YEARSLEY LECTURE
5.15 P.M. (1, Wimpole Street, W.1.) Dr. Karsten Kettel (Hillerod, Denmark): Surgery of the Facial Nerve in Atraumatic Facial Palsies.
ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW
8.30 P.M. (242, St. Vincent Street, Glasgow, C.2.) Dr. J. F. Christie, Dr. William Blair: Otitis Media.

Saturday, 7th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
11.30 A.M. Professor Wullstein: Ciliary Action of Living Nasal Mucous Membrane. (Film.)